The New England
Journal of Medicine

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VOLUME 224 JUNE 19, 1941 NUMBER 25

THE CARE OF THE HOSPITAL OUTPATIENT*

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I AM deeply appreciative of the honor that has been conferred on me by the opportunity to present this George Washington Gay Lecture on the Care of the Patient. I have accepted the invitation of your committee in a corresponding spirit of humility and with a full realization of my inability to contribute anything of importance to the masterful addresses on the art of individual medical practice already delivered in this series by Peabody, Thayer, Herrick and other distinguished clinicians. Their presentations were of such a fundamental nature and on such a broad human basis that they will stand permanently as guides in the art of medicine. Fortunately, however, Dr. Gay, being a person of wisdom and foresight, established his foundation for lectures on the economics as well as the ethics of medicine, and therefore undoubtedly anticipated a need for constant change in the organization of the profession for the provision of efficient and at the same time reasonably priced medical service. In any event, I am taking advantage of such an interpretation of his conception of the future of medicine to discuss some of the more recent developments in the care of the patient, especially with reference to its accomplishment by a group of practitioners rather than by an individual physician. This type of practice for the hospital inpatient has for a long time been well established, and, by referring more specifically to its employment in the care of the hospital outpatient, I wish to indicate its equal availability and some of the advantages of its more general use in other fields of medical endeavor.

No matter what form of practice may ultimately develop, however, let us not forget that the care of the individual patient always constitutes the primary function of the physician and that this implies more than the management of the disease from which the person suffers. Since the development of disease depends on the reactions of a person to unfavorable conditions in life, its control, including its prevention, may involve not only a consideration of each patient's innate constitution, of his physical, mental and emotional equipment, of his personality, of his habits, of his social relations and of his contacts with the physical world, but also an appraisal of all the factors, internal and external, that tend to create for him an abnormal situation. Thus, whether it grows out of the science or the art of medicine or comes from some of the related sciences or arts, every recorded observation, every established fact, every technic and every human effort that contributes to the prevention, recognition or management of a diseased state in man may be regarded as in keeping with the fundamental aim of medicine.

The accomplishment of good care for the patient, therefore, requires not only a knowledge of disease itself and of the technics for its prevention and amelioration, but also an understanding of the person who has the disease and the skill with which to apply the effective therapeutic procedures. The established facts regarding disease and its treatment may be acquired from the observation of others, and it may be assumed that you, as Harvard students, have already learned many of these from your teachers, your textbooks and the current medical journals, but to understand people and to have the skill with which to apply your knowledge to the alleviation of their ills is a far more difficult matter and is never completely mastered.

The changes in the methods of practice that are now taking place have been attributed by some to a desire on the part of the Government to socialize every phase of life, to regiment all our activities and to limit our personal freedom, but, for medicine at least, the modern viewpoint can be explained on a far simpler and more rational basis. Not so long ago the family physician was presumably instructed in all the currently known

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aspects of medicine; his patients were usually his neighbors and his intimate friends, he knew their heredity and their personal habits, and he was supposed to know, under most circumstances, what the profession had to offer for the relief of their ailments. Furthermore, when a particularly difficult clinical situation, diagnostic or therapeutic, arose he could only call in a colleague or consultant whose advice was based largely on personal experience with similar cases. No exact methods of diagnosis and no specific therapeutic procedures were available. With the development of surgery, and later of the specialties, with the great advances in the scientific knowledge of disease and especially with the development of the modern hospital, including its special facilities for diagnosis and treatment, it obviously became impossible for any one physician, no matter how well trained and equipped, to meet all the needs of some of his patients. Consultants, furthermore, instead of making a diagnosis or advising therapy on purely clinical observation of the case or on their general experience, began to demand exact scientific data, and patients themselves began to question the diagnosis and the forms of treatment that were not based on exact laboratory procedures.

It is readily admitted that in the great majority of cases the disease can be easily and satisfactorily diagnosed and managed by a competent practitioner. In fact, not only because it involves less time and expense but also for psychologic reasons, complete care by a single physician is often more effective. No system of practice, as a matter of fact, that requires useless professional activity or unnecessary procedures of any kind will serve the patient's or the public's best interest. And yet the problems of some patients are so complicated and the available means for attacking them are now so specialized that a group of physicians, many of them differently trained and equipped, must be called on to deal with the individual case. Their efforts, however, to be maximally effective must always be directed and co-ordinated by some single person, the personal adviser at least for the time being, so as to afford the patient a consistent program of intelligent care.

The importance of having at all times for each patient, no matter what the nature of his case, a competent physician responsible either for all the care that is demanded or at least for its administration by others is generally appreciated. Yet, in the process of the change that is now taking place in medical procedure, many patients have lost the kindly, continued medical supervision that constituted the chief advantage of the older system. Even in the wards of our hospitals, where all the physicians concerned are closely associated, it sometimes happens that no one of them becomes the patient's personal adviser, co-ordinates the efforts that are made in his behalf and sees to it that his emotional as well as his physical problems receive their due share of attention. About this aspect of the matter Peabody spoke most emphatically in his Gay Lecture of 1927; it demands equal emphasis today. In private practice, except perhaps with the financially well-to-do, the situation is even more serious: because of the added expense or for fear of losing the patient, the practitioner may not seek the advice of qualified specialists, or, if he does so, may not be in a position to control the further management of the case. On the other hand, the specialists involved, because of a lack of personal contact with the referring physician or with each other, may be in ignorance of important aspects of the case other than their own. Finally, the patient himself, irrespective of his financial status, may choose his own specialist, often incorrectly, or may drift from one physician to another with no correlated supervision. In the end, he may put himself in the hands of a cultist or give up in despair.

At any rate, in spite of the improvement in medical facilities, the great mass of the population is not yet receiving the good medical care that the profession is capable of supplying. Statistics concerning the supply and distribution of physicians and the number of people within or beyond their reach in the country at large vary greatly, but are of little, if any, value, since they do not indicate the type of care that is available. The unfortunate situation is better shown by the number of patients who come to hospitals, even in the large cities, with an unrecognized and hopeless cancerous lesion, with a neglected and advanced pulmonary tuberculosis, with a ruptured appendix, with a long-standing intestinal obstruction or with a severe but preventable type of infection. Too often one finds that the family physician had failed to do a digital examination of the rectum, to palpate a breast, to make a careful clinical study of the chest or to do a blood count or a simple urinalysis. I do not want to be unfair to our profession, but we must face the situation, and admit either that many of our general practitioners are incompetent to render good medical care or that the present system of practice does not permit them to render the service of which they are capable.

One cannot entirely excuse the average practitioner for such a situation, or fail to take advantage of the opportunity to urge better training for him; and yet, before we place the chief blame on the

family physician, let us remember that far more is expected of him than in the past, that he too, to an extent, may be a specialist of some sort, that his small fees limit greatly his time for the individual patient, and that once in active practice, he often has little opportunity to keep abreast of the advances in medicine.

The hope for better care of the average patient, therefore, seems to lie largely in some reorganization of the system of practice, one that would make available to the practitioner all the facilities needed for the care of his patient and at the same time permit the physician to make a good living and to do his work leisurely and effectively.

Special types of highly organized medicine have developed in response to this situation: the elaborate medical departments of the United States Army and Navy, to meet the health needs of our active soldiers and sailors; the veterans' hospitals, to care for the physical handicaps of previously enlisted men; institutions, under governmental auspices, for the supervision of the insane and the tuberculous; industrial medical units, for the care of employees and sometimes of their families; finally, various associations of physicians for the conduct of private practice, sometimes under an insurance system.

Before discussing the hospital outpatient department as a further example of this type of practice, and one that is organized to function in cooperation with the general practitioner, it is worthwhile to consider the essentials of good medical care. I think they may be summarized as accurate diagnosis, the economical and efficient employment of all the established measures of therapy, and continuous personal supervision of the patient as an individual.

Surely accurate diagnosis is the first requirement. This involves, in many cases, much more than the securing of a detailed story of the patient's symptoms, of his past medical experiences and of his family and social relations; it includes more than a meticulous physical examination and the accomplishment of a few routine laboratory tests. Frequently it necessitates, at least for purposes of elimination, the services of specially trained professional and technical workers: chemists, bacteriologists, roentgenologists, ophthalmologists, urologists, gynecologists, otolaryngologists and, sometimes, general surgeons. It requires, furthermore, that the results of the studies of these specialists be assembled and analyzed, in the light of the primary clinical observations, by someone who is highly trained and experienced in the broader aspects of clinical medicine, by one who stands in the position of "physician" to the particular patient.

The second essential for good medical care is that all the necessary facilities for the treatment of the diagnosed condition be made available to the patient. This may involve nothing more than an assurance on the part of the original physician that no disease process has been discovered, and some advice about the patient's manner of living or the regulation of his diet; but it may require the services of another special group of professional and technical workers, such as surgeons, roentgenologists, psychiatrists and physiotherapists. It may necessitate the employment of elaborate physical equipment: a roentgen-ray machine, orthopedic apparatus, gymnasiums and so forth. It may, of course, demand hospitalization of the patient.

The third and equally important requirement is continuous personal supervision of the patient throughout the period of his study and of his treatment. On the success or failure of this phase of care, which involves primarily the art of medicine, rest to a large extent the degree of cooperation of the patient and the ultimate result of the therapeutic effort. So far as possible, the doctor originally consulted by the patient should assume the responsibility for his total management. In most cases he will be the family physician, the general practitioner or the internist, but whatever his type of work, if he is capable of carrying through this aspect of the patient's care, he may be regarded as a "physician." Although I fortunately have the privilege of knowing many specialists and surgeons who are excellent physicians, I know others, even internists, who function largely as specialists, in the narrow sense of that term, having no interest in the patient beyond the management of his disease, and in that only so far as it fits into their special fields of scientific effort. Such a person, no matter what his qualifications in a special line of work, cannot be looked on in the true sense of the word as a physician. Such a specialist, to supply all the essentials of medical care to his patient, must usually function in co-operation with another practitioner, one who can assume responsibility for the general management of the patient, one who will be his "physician."

Sometimes, for special diagnostic investigations, for therapy, for personal reasons of the patient or the doctor or for a new viewpoint regarding the case, it is necessary at least temporarily to transfer the patient from the supervision of one physician to that of another, as, for example, when hospitalization is required, when the immediate disease process lies outside the range of the first doctor's activity or when an assigned professional service in a clinic or hospital terminates. Under such cir-

cumstances the transfer of responsibility should be clearly understood by the patient as well as by the recipient physician. Only in this way can a continuity of personal supervisory service to the patient be maintained and his thorough co-operation secured. Furthermore, when the situation is so managed and the activities of the second physician have been completed, the patient ordinarily should return to his former physician and thereby maintain a more permanent relation with him. Such an arrangement not only makes for consistent care of the patient but at the same time establishes and maintains a cordial relation among physicians.

I shall now discuss the hospital outpatient and consider to what extent the organization that has been developed for his care meets the indications that I have outlined, and incidentally to what extent it has failed to do so.

From one point of view, at least, the outpatient has from the start a great advantage over the ordinary private patient: like the ward patient, he does not have to pay the costs of his medical care. He may be admitted to the hospital clinic on an entirely free basis, or, if able, he may pay something to the institution, but under no circumstances are the services limited by his economic status, and there is no financial relation between the doctor and the patient. This divorce of the monetary aspects of the care of the patient from its professional phases is significant not only for the patient, but also for the physician. It frees the former from the fear of jeopardizing his economic status, whatever it may be, or of incurring financial obligations that he cannot meet; it gives the latter free rein to devote to the patient and to demand of him whatever amount of time the case deserves, to seek such laboratory and professional aid as may be needed for diagnosis or treatment, and to establish a personal relation unhampered by any thought, on his part or that of the patient, of subsequent materialistic adjustment. Under such circumstances the professional and personal aspects of the doctor-patient relation take precedence over all others and create an ideal background for good medical care.

In this connection, it may be appropriate to say a word regarding the free choice of physician, about which there has recently arisen a great deal of controversy. The hospital outpatient has no opportunity to select his physician although in many institutions if he is dissatisfied with the one to whom he has been assigned he may, on request, be transferred to someone else in the same department. In my experience such a request has rarely been made. The average patient comes or is sent by his family doctor to an institution because of its reputation in the community, and, so long as he is receiving what I have defined as good medical care, he is co-operative, quickly develops a sense of loyalty to his physician and expects no variations from the routine of the organization except as indicated by his professional needs. It is to be assumed, however, that at each visit for a reasonable period the patient sees the same physician, as he would if consulting a private practitioner, and that, in consequence, no confusion about the continuous personal management of his case develops.

Since I have defined accurate diagnosis as the first essential in good medical care, I shall now review the opportunities for exhaustive study of the patient in the outpatient department of a general hospital. The entire facilities of the hospital, so far as they can be utilized for an ambulatory patient, may be made available. This includes not only the physical apparatus, such as the roentgen-ray equipment and the laboratories, but also the entire personnel of the hospital, professional and technical. From the viewpoint of the hospital's service to its community, the outpatient department may become, perhaps is already, of even greater importance than the ward. A larger number of patients can be cared for, in most instances they are in the earlier stages of their disease and they can oftener be cured and again made useful citizens. In addition, many of the patients, except for the outpatient service, would eventually become ward cases and so require the additional expense incident to lodging and board. Furthermore, many outpatients, even while under observation, may continue their employment, and consequently at the same time be productive citizens, supporting themselves and their families. It behooves the hospital, therefore, as a public institution, to contribute to outpatients all its available resources for diagnosis and for treatment.

In some institutions only the younger and less seasoned clinicians do the outpatient work, but from the viewpoint of their service to the community the more experienced staff members, if only in an administrative or consultant capacity, might be of greater value in the dispensary than they are in the ward.

In any event, a well-organized outpatient department, co-operating freely with similar units in a general hospital and having the entire physical and personnel facilities of the institution at its disposal, is ideally equipped to afford accurate diagnosis for its patients.

As to the second essential for good medical care, that of treatment, little more need be said. If the facilities for diagnosis are available, so also

are those for treatment. This may sometimes involve the necessity for hospitalization, but it is astonishing to what extent the development of efficient outpatient departments, in addition to the advance in methods of therapy, has diminished the reference of certain patients to hospital wards. In my intern days, our wards were filled with patients of a type that are now equally or better cared for on an ambulatory basis, especially those with pernicious anemia, diabetes, peptic ulcer and gall-bladder disease, and some with cardiac, renal and pulmonary disease. Now such patients rarely need be admitted to a hospital for diagnosis, and for treatment only when the disease is well advanced or refractory or demands prolonged bed rest or surgery. From a gastrointestinal clinic I find that, although we still refer many patients to the surgical wards, only rarely is it necessary to hospitalize them for diagnosis or even for medical treatment.

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The chief difficulty in the outpatient department concerns the third essential for good medical care: continuous personal supervision of the patient. This, however, is because we have not always given proper consideration to the art of medicine in our outpatient services. Owing to the number of patients, the relatively brief period available for each one, the physician's desire to see as many of them as possible, his primary interest in the abnormalities that they present or a feeling that they are "only outpatients," the human side of their problems has been neglected. Sometimes perhaps we have been too ready to pass them on to some other department for a tonsillectomy, a tooth extraction, a gynecologic examination or some other diagnostic study, or for some form of treatment by a specialist. There the patient's association with the hospital may have ended, or he may have been sent on to another clinic, no one taking the trouble to act as his "physician."

Outpatients, however, are just as human as private ones, and although usually more easily controlled, they require an equal consideration of their personal problems. Often they go to the hospital after considerable hesitation about doing so, but they usually go because they want help, and they are keenly appreciative of any manifestation of interest and sympathy. The greater the intellectual gap between them and their physician the easier it is to establish an emotional relation: one of friendship, of loyalty, of understanding and of an obvious desire to help. To such an attitude on the part of the physician, the average outpatient readily responds with the utmost co-operation. Furthermore, it rarely requires any extra time to develop such a personal relation, for it is largely a matter of the physician's manner and of his consideration of the patient's personal as well as of his specific medical problems. The interest must be maintained, however, and must extend to the patient's management so long as he is under the physician's observation.

Some such relation with the patient should also be manifested by all those with whom he is associated. The admission clerk, the secretary, the nurse, the social-service worker, the laboratory technician, as well as the physician, should constantly maintain toward him an attitude of friendliness and of personal concern for his welfare. Any one of these, by an injudicious remark, a display of temper, an indication of prejudice, a sign of preference for one patient over another or an unkind act of any sort, may so disturb the patient as to undo the best efforts on the part of the others. On the other hand, some one of the group — oftenest a secretary, a nurse, a social-service worker or an officially designated hostess — may so impress the patient with her interest in his case and her personal desire to help him, that she may greatly simplify the duties of the physician in this regard. Ideally, if a person with such qualifications is available on the staff of a clinic, her other duties should be subordinated to this most important one. She should welcome the patient to the department, even before he meets his clinic physician, should see him again before he leaves and should discuss with him subsequent visits, detailed arrangements for consultations with other physicians of the hospital, for laboratory procedures and for hospitalization. She should also be the one to accompany him to other departments of the hospital, to visit him in the wards and often to lend moral support when an important decision — for example, regarding an operation — is to be made. In some cases she should be with him when he goes to the operating room. In such a way a single member of the staff, not necessarily and perhaps preferably not a physician, may give continuity to a patient's care and at the same time greatly relieve the professional staff.

Finally it becomes necessary to consider the ultimate disposition of the outpatient. If he has been referred by a family physician, whether merely for diagnosis or for diagnosis and treatment, the matter is not difficult. When the diagnostic studies have been completed or the indicated treatment has been given, the patient is referred back to that physician and the latter is informed, preferably in writing, of what has been accomplished. The patient is then again in the hands of his original physician, and presumably he will continue to

consult him from time to time as the occasion demands.

For the unreferred patient, however, who is usually indigent, the matter is more difficult. The hospital's duty to him is not ended until his disease is cured, or at least until his physical condition is stationary and requires no further professional observation. If he develops a subsequent illness that demands only ambulatory supervision, he will presumably return to the same hospital for reference to the proper clinic. If, however, he develops a disease that requires home care, few clinics or dispensaries are able to handle the situation. Boston, however, is fortunate in this respect, having the Boston Dispensary, the obstetric service of the Boston Lying-in Hospital and the pediatric service of the Boston Floating Hospital, all of which supply home care. Ordinarily the former outpatient, when a new illness develops and he cannot return to the clinic, calls in a local physician, whether or not he is able to pay for such special service, or he goes without medical supervision. When the physician knows that he cannot be paid, which happens with most former outpatients, it is unfair to expect him always to render what I have defined as good care; when the patient does not seek medical advice, he may not only endanger his own life but also become a menace to his family and his community. The care of the indigent is not, therefore, as yet completely solved, even by most hospital outpatient departments.

Thus even in the large cities, where the hospitals are well staffed and equipped and the outpatient services are well organized, some of the problems of the patient who cannot afford to pay for medical attention remain unsolved. How much more acute must this problem be in the small cities and the rural communities, in some of which no hospital exists, or at least none with provisions for the complete study and treatment of the ambulatory patient. His medical care, under such circumstances, depends not on the community at large but on the charity of the local medical profession.

One is led, therefore, on the basis of these considerations of hospital outpatient service, to speculate on the extent to which the principles that I have discussed may be applied to the supervision of the private patient of moderate means. He does not expect, nor is it desirable from his or a public viewpoint, that his medical services should be secured on a charity basis, and yet it is highly important that he have the opportunity to secure at least as good care as the hospital outpatient. This implies that all the facilities for an accurate diagnosis, for comprehensive treatment and for continuous personal supervision by a physician be made available to him. The chief difficulty is an economic one. Its solution seems to lie in some plan by which the cost can be kept within his means. Various experiments along this line have been developed: formally organized clinics, including a hospital, such as that of the Mayos, in which the cost is carefully adjusted to the patient's ability to pay; pay and part-pay clinics, such as those of some of our large general hospitals, to which patients of a limited income are admitted; specially constituted groups of private physicians, largely for office practice, such as have developed in our western states; and less formally organized groups of physicians, such as the Boston White Cross, in which each physician functions independently, except that the usual fees are replaced by payments from a pooled income, which is derived from periodic and special-service contributions by the subscribing members. Although in the past the individual doctor cared for all the patients in his community, irrespective of their ability to pay, and evened up his income by good fees from the more affluent, the present tendency is to charge each enrolled person the same fee, irrespective of the amount of service required. Any of these systems leads to a controlled distribution among the physicians of the total professional income, but perhaps to a more equitable distribution, because it may be based on merit and the type of service rendered. Such an arrangement should prove especially attractive to the well-trained younger men in the profession, because they are in great demand by such groups and because from the beginning they can be assured of a reasonable income, of an association with older and more experienced practitioners and of more regular hours of work.

In spite, however, of the obvious advantages of group practice for those of moderate means or even of the wealthier classes, it must constantly be remembered that in at least one important respect it differs from hospital outpatient service: its financial aspect. The members of a hospital staff are on a salary or give their services without remuneration. Whatever compensation they may obtain bears no relation to the number or kind of patients cared for or to the type of service rendered. On the other hand, in the private group, large amounts of money are often handled, its distribution is determined more or less arbitrarily, opportunities for unfairness and discrimination arise, and personal jealousies among the participants not infrequently develop. I do not wish to discuss this phase of private group practice, but merely to call attention, in connection with it, to the importance of honest and open financial arrangements that will prevent unfair practices,

such as fee-splitting, the unnecessary use of professional and technical facilities and questionable advertising.

Any such plan for the care of the patient of moderate means by a group of physicians and on a prearranged cost basis need not, however, interfere with a continuance of private practice, as now understood, so long as the other more favorable features of group care are in some way maintained. Many of the patients with an easily diagnosed and simply treated disease can, of course, be adequately managed by the practitioner functioning alone, but unless he has intimate association with a variety of physicians whose training and skills are along lines other than his own, unless ample technical assistance and physical equipment are available either to him or to his associates and unless he has the free time to take advantage of opportunities for reading and for study of the new developments in medicine, he is likely to fail in the provision of the best possible service for his other and more difficult cases. Evidence of an appreciation of the importance in private practice of such professional associations, such mechanical aids in diagnosis and treatment and such continued education is now apparent in the tendency of the physician to seek offices in a hospital or professional building, where these associations and physical facilities are available, in his interest in postgraduate courses of study and in the rapidly mounting membership of our national societies.

Finally let me emphasize, however, that, no matter what the organization for the practice of medicine, its ultimate success depends on the training, the skill, the intelligence and the character of the individual physician and especially on his capacity to render sympathetic, continuous and personal service to the individual patient.

Many other interesting aspects of the care of the patient readily present themselves, but my purpose today has been merely to arouse your interest in some of the broader problems and to indicate to what extent the present practice in the outpatient departments of our hospitals has already shown a solution of them. I trust that it may lead some of you to a determination not only to be proficient in the science and the art of medicine but also to strive to perfect for the public better facilities for good medical care.

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PAIN IN CANCER OF THE FACE, JAWS AND NECK*

An End-Result Study of the Relief Afforded by Neurosurgical Methods

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IT HAS been generally believed that pain associated with cancer of the face, jaws and neck can be permanently relieved by some neurosurgical procedure whenever the patient and the doctor make up their minds to have it carried out. Furthermore, except by those who are familiar with the intimate details of cancer therapy, it is also widely assumed that the pain associated with cancer in these locations is traceable to the disease and not to the methods used in treating it. Based on these assumptions, operations that denervate the diseased areas have always been held in reserve until the last possible moment. This report of an end-result study of 30 cases of cancer demonstrates the inaccuracy of both hypotheses. Superficially the findings are most discouraging, but they emphasize, nevertheless, certain fundamental truths that can be expected to point the way in the future to not only greater comfort for these patients but also to the promise of greater efficiency in cancer therapy.

All these patients were referred to me for relief of pain. Except so far as it was required by such emergencies as a sudden hemorrhage, the therapy, while the patients were under my care, was directed toward that end alone. Fourteen cases came from the Collis P. Huntington Memorial Hospital. Four patients died while under treatment. One of these was not operated on but developed a fatal inhalation pneumonia in two weeks; another died from peripheral circulatory collapse associated with tuberculosis and cancer of the cervical lymph nodes and cancer of the lung and mediastinum; the third died because of cachexia and carcinomatosis; and the fourth death followed a ligation of the carotid artery for hemorrhage. Although all the others were asked to do so, only 3 patients returned to the Huntington Memorial Hospital for further care after their discharge from my wards. Three went to other public institutions, 3 made no further hospital visits anywhere, and 1 has been lost. Twelve patients were referred

*Read at a meeting of the New England Cancer Society at the Collis P. Huntington Memorial Hospital, Boston, November 7, 1940 (the statistics are corrected to June 1, 1941).

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by other members of the staff of the Boston City Hospital, 3 by the tumor clinic of the Boston Dispensary, and 1 by an outside consultant. Six died while under my care in the hospital. Two of these died within forty-eight hours as the immediate result of the neurosurgical operation. Three others died fifty, sixty and ninety days after operation respectively from a combination of emaciation and carcinomatosis; the sixth died of novocain poisoning while being prepared for operation. One left against advice without treatment, and 1 was lost track of. Four others were followed at the Huntington Memorial Hospital, the Pondville Hospital and the Boston City Hospital and by the local doctor, and 4 are still in the hospital under my care. The neurosurgical hospital mortality of the entire group was 27 per cent (Table 1).

TABLE 1. *Mortality in Relation to Sex and Age.*

CLASSIFICATION	NO. OF CASES	IMMEDIATE RESULTS AFTER NEUROSURGERY			LATE RESULTS AFTER NEUROSURGERY		
		LIVING	DEAD	MORTALITY %	STILL LIVING	LOST	LONGEST OTHER SURVIVAL
All cases	30	22	8	27			
Sex							
Male	26	18	8				
Female	4	4	0				
Age							
Under 50 yr.	4	4			1 (2 mo.)		4 yr.
50 to 55 yr.	5	3	2				19 mo.
55 to 60 yr.	5	3	2		1 (3 yr. 7 mo.)		13 mo.
60 to 65 yr.	6	4	2			1	17 mo.
65 to 70 yr.	5	4	1			1	7 mo.
70 to 75 yr.	2	2					4 mo.
75 to 80 yr.	1		1				
80 yr. and over	2	2					7 mo.

TABLE 2. *Prevalence of Metastases.*

PRIMARY SITE	NO. OF CASES	NUMBER OF CASES WITH METASTASES					
		NONE	NECK	FACE	CHEEK	PHARYNX	CHEEK AND LARYNX
Tongue	8	1	6				1
Jaw	4		2	1	1		
Neck	5	3		1		1	
Cheek	4	3	1				
Lip	2		2				
Larynx and pharynx	2		2				
Tonsil	2		2				
Parotid	1		1				
Lung	1		1				
Stomach	1		1				

There were 8 cases of cancer of the tongue (Table 2). Six of these patients had metastases in the neck, 1 in the cheek and larynx, and 1 had no metastasis. There were 4 cases of cancer of the lower jaw. All had metastasized — 2 to the neck, 1 to the face, and 1 to the cheek. There were 5 cases of cancer in the cervical lymph nodes. In 2 the source was unknown, 1 was metastatic from a melanoma of the finger, and the other 2 were cases of Hodgkin's disease. One of the first 2 had an extensive metastatic growth involving the pharynx and larynx, and 1 of the last 2 had a metastasis in the face, but the others did not extend beyond the neck. There were 4 cases of carcinoma of the cheek. This was the most favorable type. Only one had metastasized locally, and that was to the neck. Two cases each of cancer of the lower lip, the larynx and pharynx and the tonsil had all metastasized to the neck. One case each of cancer of the parotid gland, stomach and lung had metastasized to the neck. Thus, it will be seen that with the possible exception of 3 patients with cancer of the cheek and 1 with cancer of the tongue, these 30 patients had far-advanced local disease before being referred for neurosurgery.

Furthermore, it is significant (Table 3) that although 23 patients (77 per cent) went to the general surgeon for treatment of their cancer within twelve months of their first symptom — 18 within six months — and 16 (53 per cent) had their first pain within that period, only 11, or 37 per cent, were referred for neurosurgical therapy within a year of their first symptom, and only 4, or 13 per cent, within six months. This strongly suggests that although patients with cancer of the face, jaws and neck go early to the doctor for treatment and develop their pain early and while in the doctor's care, they are not referred for surgical relief of that pain until considerable additional time has elapsed.

So far as this series is concerned, neurosurgical relief of pain was withheld until the cancer was

far advanced and complicated by extensive local metastases and until after 17 per cent of the patients had had their pain for more than a year, and four fifths for six months or more.

Neurosurgical relief necessarily carries some risk, which should be evaluated before subjecting the patient to operation (Table 4). In this group of 30 patients, 21 were operated on. Five of these died — a mortality of 24 per cent. Two died of cerebral embolus, twelve and forty-eight hours after operation. One patient died of circulatory failure seven days, and 2 others of carcinomatosis fifty and ninety days after operation. Thus, 2 deaths may properly be considered as operative, and the risk of the procedures used justly assessed at 10 rather than 24 per cent.

The only constant factor that could be regarded as a possible cause of pain in this series of patients was radiation therapy (Table 5), which was given by x-ray in every case but one in which interstitial radiation was also used. Twenty-seven patients were treated, and this form of therapy was studied in relation to the onset of pain. In 10 cases, the onset of pain preceded treatment by x-ray. A statement was made by one of these patients that the radiation relieved her pain. However, this was the only time that such a claim was advanced. In 17 cases, the pain followed x-radiation, having usually a cause and effect relation in the patient's mind. In 3 cases, no radiation therapy was given. The denervation was performed as the primary step in the treatment of the cancer in 1 of these cases. Thus, in 57 per cent of these patients, x-ray therapy of the cancerous area cannot be ruled out as the cause of the local pain. The pain was widespread in its distribution. It did not necessarily conform to dermatomic areas. This is to be expected considering the extent of the neoplastic process in practically all cases. The pain involved the face, neck, ear, mouth and head most frequently and in that order. It was located in the face alone twice, and in the neck, ear and mouth alone once each. In all other patients, at least two and often three and four adjoining regions were affected.

This distribution increased the difficulty necessarily met with in reaching a decision concerning the area that should be denervated. Although a variety of operations had to be done, all but one concerned the fifth and ninth cranial and the upper cervical nerves alone or in some combination. In this one case, the spinothalamic tract was divided in the medulla at the level of the top of the olive, the second and third cervical roots were cut bilaterally, and the accessory portion of the spinal accessory nerve was divided on one side in addition. This patient is still in the hospital five months after the tractotomy and two months after the other procedure because of the increasing disability produced by the cancer. He has had a large measure of relief. The most frequent procedure was section of the sensory root of the fifth nerve by the transtemporal route. This was done twelve

TABLE 3. *Relation between First Symptom, Onset of Pain and Neurosurgical Consultation.*

TIME	NUMBER OF CASES PER PERIOD							
	CUMULATIVE				NONCUMULATIVE			
	No interval	Less than 6 months	6 months and under	1 year and under	Over 1 year	Over 2 years	Over 5 years	Total greater than 1 year
Interval between the first symptom and the date of the first treatment	9	14	18	23 (77%)	4	1	2	7 (23%)
Interval between the first symptom and the onset of pain	3	9	9	16 (53%)	8	3	3	14 (47%)
Interval between the first symptom and the date of the neurosurgical consultation	0	4	4 (13%)	11 (37%)	5	9	4	18 (60%)
Interval between the onset of pain and the neurosurgical consultation	0	16	17	24 (80%)	2	2	1	5 (17%)

TABLE 4. *Risk and End Result of Operation.*

CLASSIFICATION		NO. OF CASES	
All cases			30
Survivals		6	
Deaths	(73%)	22	
Lost		2	
Deaths			22
In the hospital		10	
In 48 hours		2	
Others		8	
Operated cases	(10%)	2	
After discharge		12	
Effect of operative therapy			
Relief			13
No relief			12
Still under treatment			4
Left against advice			1

TABLE 5. *Pain in Relation to X-Ray Therapy.*

DEVELOPMENT OF PAIN	LIVING PATIENTS	DEAD PATIENTS	TOTAL
Before x-ray therapy	7	3	10
After x-ray therapy	13	4	17
No x-ray therapy	2		2
Neurosurgery before x-ray therapy	1		1

times, two being complete and the others being differential sections. The fifth and ninth cranial nerves were divided or pinched through a posterior approach in 3 cases. In one operation, both nerves were divided, and in the other two the ninth was divided, and the sensory part of the fifth squeezed in a hemostat. The combination of the ninth cranial nerve and the upper three posterior cervical roots on one side was divided twice; these structures and the fifth nerve in addition were divided once. For these procedures, the approach was through a combined cervical laminectomy and hemioccipital craniotomy. In addition, 1 patient had a high (second cervical) chordotomy, and 1 a division of the cervical plexus in the neck.

Complications that influenced the choice and efficiency of the neurosurgical procedure were as follows: 2 patients, 1 of whom died, had a paralyzed larynx; 3 had osteomyelitis of the jaw (1 died); 3 had severe bleeding from the cancer; 2 had demonstrable brain and abdominal metastases (1 died); 2 had active local infections, one of which extended into the operative wound; 1 had a complete peripheral facial palsy on the involved side; 1 had an idiosyncrasy toward novocain (previously unknown) and died from that cause as he was being prepared for operation; and 2 were obviously very bad surgical risks.

The immediate results of the operative therapy were good and appeared to promise well for the future. Twelve patients were not relieved. Ten were not operated on, and 2 died within forty-eight hours of operation. One left against advice without treatment, and 1 was relieved by cobra venom for a month. One was relieved of pain but had severe cerebellar symptoms after operation, 13 were comfortable when they left the hospital, and 4 are still in the hospital following operation. Thus, of these 21 patients subjected to neurosurgical procedures, 13, or 62 per cent, were discharged from the hospital or died in the hospital relieved of pain. Of the 9 not operated on, 2, or 22 per cent, were relieved for a month or more. Within six months of their discharge, two thirds of this group had died. One may conclude, therefore, that at the time of leaving the hospital following treatment for pain, the patient with extensive cancer of the face, jaws and neck has almost 50 per cent greater chance of getting relief if he is operated on than he has with nonoperative therapy. Furthermore, since 41 per cent of the operated patients lived longer than six months after seeking neurosurgical relief, whereas only 22 per cent of the nonoperated group survived for the same period, it cannot be argued that the risk of operation is a deterrent to surgery. This immediate success attendant on denervation therapy doubtless accounts for the widespread belief in its efficacy, even when it is used inexcusably late in the course of the disease.

Twenty-four patients were followed to an end result of either death or established relief of pain (Table 1). The longest follow-up period was four years. So far as is known, this patient, who was not operated on, died unrelieved in Ireland. The shortest period was two months. This patient was not operated on and had partial relief following the drainage of an abscess in a carcinomatous mass in his neck. Two patients — both operated cases and both relieved of pain at their discharge from the hospital — have been lost. Four others are still under treatment in the hospital.

Only 1 of the remaining 22 patients is alive today. This one survivor — and this is the only such case in the entire group — is completely relieved of both pain and cancer three years and seven months after his neurosurgical operation and five years and one month after his first symptom. This man, who was referred by Dr. Charles Lund, was fifty-nine years of age and had a cancer of the cheek without local metastases. His pain started a year and three months after his first symptom and followed x-ray therapy. He was denervated three months later by division of the fifth and ninth cranial nerves in the posterior fossa. He was invalided for a number of months by cerebellar symptoms, but these have since disappeared. The relief of his pain was complete immediately after the operation and has remained so. The only other patient with a significant survival period is a woman of sixty, who also had a cancer of the cheek without local metastases. She was referred by the Huntington Memorial Hospital. A differential section of the sensory root of the fifth nerve was done five years after the start of pain and eight years after the first symptom. This patient's pain started before she received x-ray therapy and, indeed, was relieved by the first radiations. She had relief of pain for fifteen months after she was operated on. The tumor recurred, and she died in pain two months later.

Two other patients had complete relief for a short time before dying of their cancer; one for two months and the other for seven days. Both had local metastases. The patient with cancer of the parotid gland obtained no relief from division of the ninth and upper cervical nerves, and subsequently went to Philadelphia, where she received treatment by refrigeration. This also was not successful, and she eventually died thirteen months after the neurosurgical operation. Every other patient is dead or still under treatment. Of the former group, one lived for nineteen

months, but all the rest died within seven months after neurosurgical treatment. All died in pain and with no more than very temporary relief from these procedures.

Certain conclusions relative to the treatment of the pain associated with cancer of the face, jaws and neck seem to me to be inescapable. These are that little if any relief can be expected from either medical or neurosurgical procedures that are initiated after the cancer has metastasized locally. If, despite that fact, surgical denervation is decided on, however, it carries no greater immediate risk than medical therapy and offers a much better chance of affording temporary relief.

It also seems reasonable to assume that therapeutic radiation of the malignant area is a significant factor in the causation of the pain that develops in association with cancer of the face, jaws and neck. Based on that assumption, the purpose, extent, effectiveness and pain-producing possibilities of any proposed x-radiation, as well as its relation to the possible effect that it may have on the cancer, should be carefully assessed in advance. It should never be countenanced when its effect is uncertain, or if this treatment is proposed because all other forms of therapy have been recognized as being useless.

Despite the discouraging results experienced in this series of patients, I am convinced that neurosurgery has its place in the treatment of cancers of the head and that it will prove useful when properly applied to this problem. The success following the early or premetastasizing denervation of the malignant area in 2 cases should be neither overlooked nor ignored. Under similar circumstances, it should be possible to duplicate this success in other patients. This will be possible, however, only when it is recognized that denervation of the cancer-bearing area *must* precede the development of local metastases. This will mean that, as the malignancy of the tumor increases, the need for early effective denervation increases likewise, a requirement that if carried to its logical conclusion will, in certain cases, doubtless mean complete denervation by neurosurgery before the pain develops. This procedure was carried out in 1 case in this series. This will apply particularly to those cases that require large amounts of radiation, and offers not only the promise of future freedom from pain but, because of the local anesthesia associated with the denervation, the expectancy of greater efficiency in the treatment of cancer.

Summary

The effect of neurosurgical procedures on the pain associated with cancer of the face, jaws and neck is analyzed.

Thirty cases are reported, in only 2 of which the patients had relief and were alive at the end of any significant follow-up period.

Evidence is presented to demonstrate that the development of pain in such cancer-bearing areas is associated with x-ray therapy.

Neurosurgical or any other procedures will almost certainly prove to be useless in the relief of this type of pain if provided only after the cancer has metastasized locally.

It is strongly recommended that surgical denervation of the cancer-bearing areas in the face, throat, neck and jaws be performed as the first step in the treatment of the malignant growth, not only as a prophylaxis against later pain but also as an aid to greater efficiency in the therapy of the cancer because of the associated local anesthesia that is thus produced.

ASPIRATION BIOPSY, WITH A DESCRIPTION OF A NEW TYPE OF NEEDLE*

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ASPIRATION has undoubtedly been used to withdraw fluids from various parts of the body ever since hollow needles were first added to the medical armamentarium, but the use of aspiration to obtain specimens from solid masses has a much shorter history. About 1900 Dr. Samuel Mixter, of Boston, devised a biopsy punch that is still in use at the Massachusetts General Hospital to obtain specimens from brain tumors.[1] It consists of a hollow needle fitted with a blunt-nosed obturator, and has a hub that will receive the tip of a syringe for aspiration of tumor tissue. Figure 1 shows three models of this punch. Grieg and Gray[2] used aspiration biopsy to obtain specimens from lymph nodes as early as 1904. Guthrie,[3] in 1921, reported the use of aspiration biopsy of lymph nodes and Barringer,[4] in 1922, described a needle with a small cutting screw at the point, devised by Goeller, with which specimens were withdrawn from the prostate in cases in which the diagnosis was in doubt. Martin and Ellis[5] state that needle biopsies have been used at the Memorial Hospital in New York since 1926. In 1927 Forkner[6] described the use of needle biopsy at the Collis P. Huntington Memorial Hospital in Boston to obtain material from lymph nodes. He used a dental broach, constructed on the principle of a fishhook, which he passed through the lumen of a 17-gauge or 18-gauge needle to secure more material than he could with the needle alone. Needle or punch biopsies did not come into common use, however, until about ten years ago, when the advantages and possibilities of the method became more widely recognized.[5, 7–18]

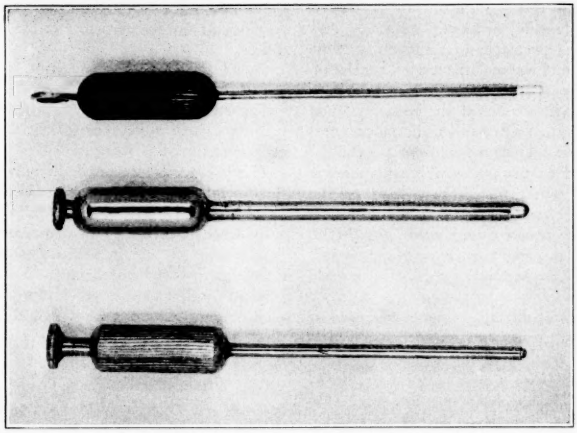

FIGURE 1. *Three Models of Mixter's Biopsy Punch.*

Biopsy by aspiration through a large-bore needle has been more successful in obtaining specimens from deep-lying tumors than biopsy by a punch, since the latter often loosens pieces of tissue, especially in cellular tumors, the removal of which is not always successful. Aspiration with a syringe provides a good means of withdrawing a piece of tumor tissue, once it has been loosened, but difficulty is often experienced in causing a fragment of tumor to be loosened with the ordinary needle. No entirely satisfactory combination of a punch and aspiration has yet been devised because of the problem of making a mechanically satisfactory punch within the lumen of a needle in a size within practicable limits.

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An ordinary needle of 14 to 18 gauge with a tightly fitting syringe of 5-cc. to 20-cc. capacity often suffices to obtain a satisfactory specimen of a tumor, and enables the pathologist to make a diagnosis. Usually, however, only a few isolated tumor cells or small groups of cells can be obtained.

piration biopsies, and have used it for about two years with considerable success. It was devised to obtain larger fragments of tissue, and at the same time to keep the needle simple and inexpensive.

By taking a 14-gauge needle with the obturator

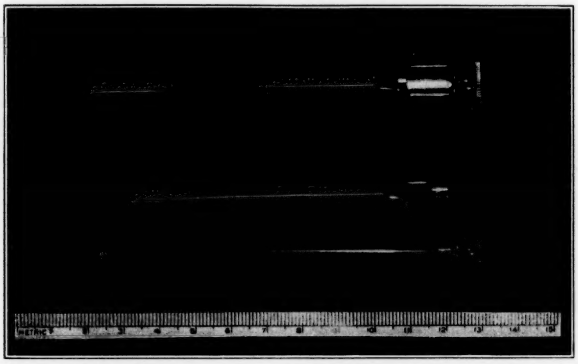

FIGURE 2. *Two Models of the Author's Needle for Aspiration Biopsy. The lower one, with obturator withdrawn, is provided with a Luer–Lok hub.*

With experience, some pathologists are willing to make a diagnosis on this meager material, but the problem is admittedly made easier when a larger specimen is provided for a study of the structure

FIGURE 3.
Detail of the tip of the author's needle, with the obturator withdrawn (A) and inserted (B).

of the tumor as well as of the individual component cells.

Dissatisfaction with the material secured by needle biopsy is evinced by the introduction of numerous new models of punches and needles, each designed to obtain larger specimens. Punches or needles were developed by Hoffman[19] in 1931, Hoffman[12] in 1933, Lindblom[20] in 1935, Lowsley[21] in 1935, Corriero[22] in 1937, Neumann[23] in 1938 and Silverman[24] in 1938.

I have also designed a needle (Fig. 2) for as-

in place and making three bevels at the point, instead of the usual single bevel, a trocar point is made, and when the obturator is withdrawn, the needle is left with three cutting teeth (Fig. 3). When the needle is rotated, the teeth act as a trephine to core out pieces of the tumor. If suction is provided by a syringe simultaneously with the rotation, the loosened fragments are easily removed.

After application of an antiseptic to the skin, a wheal is made with novocain solution, and a minute stab wound is made with a sharp-pointed knife blade. The needle, with its obturator, is introduced until it is felt to engage the periphery of the tumor. The obturator is then withdrawn, leaving the three-toothed sheath in position. A 10-cc. or 20-cc. syringe is attached, and the plunger partly withdrawn to produce a vacuum. The plunger is grasped between the fifth finger and the hypothenar eminence of the right hand, and the thumb and index finger rest against the rim of the barrel of the syringe to hold the plunger partly withdrawn to maintain the vacuum. The barrel of the syringe and the needle are then rotated as a unit with the left hand and advanced into the tumor, whereas the right hand still holds the plunger tightly but permits the rim of the barrel to rotate between the thumb and forefinger.

Small pieces of tumor tissue are thus cored out, and the loosened fragments, together with some blood, are drawn into the shaft of the needle. The needle is advanced to the opposite side of the tumor, and the syringe and needle then drawn back out through the skin while suction is maintained. On reaching the skin, air rushes in through the needle and carries the fragments of tissue into the barrel of the syringe. The plunger is withdrawn, and the pieces of tissue mixed with blood are scraped out upon a large piece of hard fine-grained filter paper. The liquid portion of the material is absorbed by the filter paper. With a Beebe loupe having a magnification of two and one-half times, the specimen is carefully examined, and the pieces of tissue are teased out from the blood clot with a very fine pair of forceps or with dissecting needles and placed in a heap on a small piece of filter paper. With the magnification provided by the Beebe loupe, the fragments of tissue stand out clearly in the blood clot. The tissue amassed on the small piece of filter paper is then placed in 10 per cent formalin or Zenker's solution and subsequently prepared in the routine manner for histologic examination.

If the connection between the syringe and needle is not tight, the needle may become loosened by the rotating motion and the vacuum destroyed. To eliminate this difficulty, a Luer–Lok needle-hub and syringe may be used, and the rotation made in the direction in which the lock is tightened.

A 10-cc. or 20-cc. syringe is most satisfactory for aspiration. A 5-cc. syringe may be used, but strong suction is more difficult to maintain with it. Larger sizes are more awkward to handle. A disadvantage of many syringes is the small size of the lumen of the tip of the syringe, often considerably smaller than the lumen of the needle used. The pieces of tissue may, under these circumstances, be held up at the tip of the syringe. This difficulty may be eliminated by using a metal-tipped syringe, which is not only stronger, but permits an instrument maker to enlarge the hole in the tip if it is too small. Attention should therefore be paid to this point in purchasing a syringe for use in aspiration biopsies.

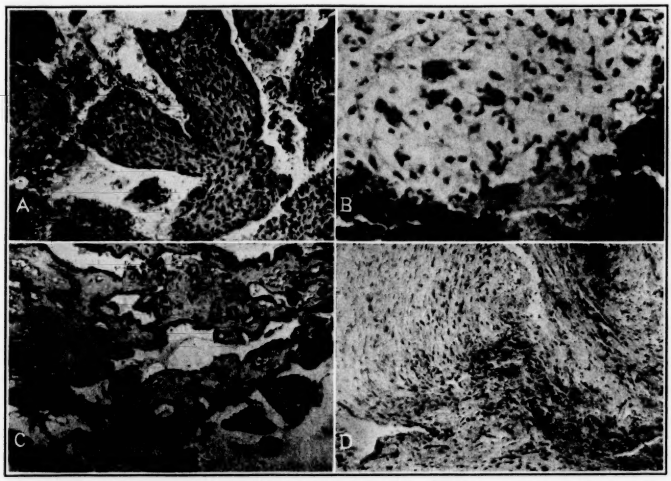

FIGURE 4. *Representative Biopsy Specimens Obtained by Aspiration.*

A. *Metastatic epidermoid carcinoma in a cervical lymph node (× 230).* B. *Metastatic hypernephroma in the sternum (× 310).* C. *Papillary adenocystoma of the thyroid gland (× 230).* D. *Fibroma of the thigh (× 85).*

The method described above has been quite successful, and has, on occasion, succeeded when attempts to obtain a specimen by using an ordinary needle have failed (Fig. 4). It has proved more successful than an ordinary needle in obtaining specimens from tumors with a fibrous stroma.

INDICATIONS FOR ASPIRATION BIOPSY

Aspiration biopsy is employed with great circumspection, and the indications for its use have

gradually become more clearly defined. In ulcerated and superficial tumors, biopsy can satisfactorily be done by removal of a specimen by the usual methods from the surface. Aspiration biopsy, therefore, finds its place in nonulcerated and deeplying tumors. It is of greatest use in confirming the clinical diagnosis in inoperable tumors, usually antecedent to irradiation treatment, and it should not be employed in operable lesions unless the needle tract can be made to lie wholly within the tissue that is to be excised.

In cases of inoperable tumor, aspiration biopsy is often indicated for pathological confirmation of clinical diagnoses. By aspiration biopsy a specimen is obtained from many tumors that would otherwise have no biopsy because of the complexity of the procedure by the usual surgical methods, because of the prolonged hospital stay and additional expense or because of the patient's refusal through fear of a surgical procedure. Many patients have an aspiration biopsy performed in the outpatient department, and need not be admitted to the hospital for treatment until the pathological report has been returned. Many hospital days are saved by this practice, an important consideration when the number of beds available for treatment is very limited. An additional advantage is that irradiation treatment may be proceeded with at once after a diagnosis has been confirmed by aspiration biopsy. After biopsy by surgical incision, on the other hand, it is advisable in many cases to postpone treatment for several days, so that healing of the wound is not interfered with when large doses of x-ray or radium are planned.

Aspiration biopsy is exceedingly useful in confirming the presence of metastatic cancer in inoperable lymph nodes antecedent to irradiation treatment when the primary lesion is unknown, when it is inaccessible or less accessible to biopsy, or when it has previously been removed elsewhere and a pathological report is not available. These circumstances occur most commonly in cervical lymph nodes. When there is doubt whether enlarged operable cervical lymph nodes are involved by metastatic carcinoma in lesions of the lip and mouth, it is preferable to do a neck dissection without preliminary aspiration biopsy, if the primary lesion is controlled.

Aspiration biopsy is used only rarely when a diagnosis of lymphoma is suspected, since in the diagnosis and sub-classification of tumors of this group it is desirable to have the architecture of the entire lymph node available for pathological examination. In these cases, therefore, a biopsy by surgical excision of a lymph node should always be performed.

In tumors of the parotid gland, aspiration biopsy is indicated only to confirm the diagnosis in inoperable tumors. If the tumor is operable, aspiration biopsy is contraindicated, since the complete specimen will be available for examination after excision, and spilling the cells along the needle tract by aspiration biopsy cannot be done without risk of recurrence unless the entire tract can be removed with the subsequent excision of the tumor. In cases in which the differential diagnosis between a malignant and a benign parotid tumor must be made, aspiration biopsy yields inadequate information.

In breast tumors, aspiration biopsy has also been reserved largely for inoperable lesions that it is planned to treat by irradiation. Carcinomas of the breast that are accompanied by inflammation fall into this class, since in these cases difficulty is often experienced in the healing of the wound of an open biopsy. In differential diagnosis of benign and malignant lesions of the breast, too frequently only a small focus of carcinoma in an otherwise benign lesion occurs, and an aspiration biopsy should not be relied on to find it. In these cases surgical exploration and frozen section are more reliable procedures. It has been suggested in the literature that aspiration biopsy is useful in determining whether or not palpable axillary nodes are involved in carcinoma of the breast. However, this does not seem to be a proper indication for aspiration biopsy, since in every operable carcinoma of the breast, the axillary lymph nodes should be removed whether they are palpable or not, because of the fallibility of clinical examination in judging whether metastasis has or has not occurred.

Aspiration biopsy has been reported to be of value in obtaining specimens from lung tumors. For this purpose I have used it to a very limited extent, because this procedure should be reserved for confirmation of the diagnosis in patients in whom no attempt at surgical removal is planned, and because of the risk of implantation in the chest wall and pleural cavity.

I have not used aspiration biopsy for abdominal tumors, since biopsy under direct vision through a small incision or through the peritoneoscope is a safer procedure.

Needle and punch biopsies have from their beginning been found useful in securing specimens from carcinomas of the prostate gland because of the difficulty in obtaining specimens by open operation when confirmation is desired. Although failure to obtain a satisfactory specimen may frequently occur, a successful result may save the patient a major operative procedure.

A carefully performed aspiration biopsy may occasionally be used with benefit in bone tumors if the history, physical examination and roentgenographic and blood chemical studies still leave doubt concerning the therapeutic procedure indicated. However, in tumors of the bones of the extremities, it is safer to perform an open biopsy distal to a tourniquet, to examine a specimen by frozen section and to amputate, if indicated.

There is rarely the need for an immediate diagnosis of a tumor by smear. Such diagnosis is rarely an emergency, and the pathologist should be given the opportunity for more careful study of larger specimens. The occasional desirability of an immediate diagnosis usually comes on the operating table, where a frozen section should be made available.

It should be emphasized that failure to obtain a positive pathological report by aspiration biopsy should not be interpreted as meaning that no tumor is present, or that the tumor, if present, is benign. Only a positive pathological report is significant.

Summary

A needle employing the principle of the trephine is described for use in obtaining biopsy specimens by aspiration.

The greatest use for aspiration biopsy has been found in confirming the clinical diagnosis in inoperable tumors antecedent to radiation treatment.

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SPONTANEOUS RUPTURE OF THE SPLEEN IN INFECTIOUS MONONUCLEOSIS

Report of a Case

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THAT rupture of the spleen is not a rare event is attested by the frequency with which such cases are reported. Although trauma, both severe and slight, heads the list of causes, one finds mention of the following conditions as etiologic factors: malaria, typhoid and typhus fever, echinococcal cyst, influenza, leukemia, polycythemia vera, hepatic cirrhosis, subacute bacterial endocarditis, tuberculosis, hemophilia and various acute infections. There are also many reports of spontaneous rupture of normal spleens.

In 1932 Attlee[1] reported a case of spontaneous rupture of the spleen in a twenty-three-year-old woman in whom a diagnosis of Vincent's angina had been made. From the clinical and laboratory reports, it seems highly probable that this was an unrecognized case of infectious mononucleosis. Aside from this case, the literature contains no report suggesting rupture of the spleen in this condition. In view of the rarity of pathological reports concerning infectious mononucleosis, the following case is of sufficient importance to be reported.

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Case Report†

R. S., a 23-year-old consulting engineer, was admitted to the Heywood Memorial Hospital in Gardner, Massachusetts, on October 20, 1937, complaining of severe abdominal pain. Two and a half weeks before entry, he developed headache and tender cervical lymph nodes. One week before entry, he consulted a physician because of a very sore throat. The throat was found to be in-

†Reported through the courtesy of Drs. Harold C. Arey and Albert F. Lowell, of Gardner, Massachusetts.

flamed, and the postcervical lymph nodes were enlarged and slightly tender. The patient continued to work, although he felt very miserable, and experienced two shaking chills the day before entry, with profuse sweats that night. The morning of entry he got out of bed to go to the toilet, and was seized with a sudden agonizing pain in the abdomen radiating up to the sternum and through to the back. A physician was summoned and found the patient in semishock, sweating profusely, with a pulse of 90 and a temperature of 97°F. He was taken to the hospital at once, and although extremely weak, he was able to walk to his room.

Physical examination showed the patient to be pale and sweating; he suddenly vomited blood-streaked mucus. The pulse was 100, the blood pressure 130/65, and the temperature 98°F. The postcervical lymph nodes were enlarged and tender. The pharynx was inflamed and beefy, with two minute ulcerations on the posterior wall. The soft palate was inflamed and swollen. The heart and lungs were normal, although the patient complained of substernal pain on deep inspiration, referred to the back. The abdomen was tense over the epigastrium, with generalized tenderness in both flanks, more on the left, and the patient complained bitterly of generalized crampy pain, most intense in the epigastrium. The urinary bladder was distended, and the patient was unable to void. Neurologic examination was negative.

During the afternoon of the day of entry the patient's pulse rose to 110, the systolic blood pressure fell to 100, the temperature rose to 100°F., and the abdomen became distended and rigid, with marked generalized pain and tenderness demanding laparotomy. Operation seemed advisable, and when the peritoneum was opened, a large quantity of free blood containing clots was encountered. The appendix, which was found to be large and to contain a concretion, was removed. The spleen was felt on exploration to be markedly enlarged, and was exposed through a second incision. The capsule was seen to be ruptured and to be draining blood freely. The spleen was removed. The surgical convalescence was entirely uneventful. The throat inflammation, however, was rather slow in clearing up, and a moderate generalized lymphadenopathy was noted. The patient was discharged 3 weeks after entry, and in another 3 weeks was able to return to work, entirely recovered. Three years later he is reported to be well.

The results of the blood examinations are given in Table 1. The preoperative blood films showed the platelets to be normal in number; postoperatively they were markedly increased. The sheep-cell agglutination test for infectious mononucleosis was positive in a dilution of 1:1256.

TABLE 1. *Blood Examinations.*

DATE	RED-CELL COUNT	HEMOGLOBIN (NEWCOMER)	WHITE-CELL COUNT	DIFFERENTIAL COUNT						
				NEUTROPHILS	EOSINOPHILS	BASOPHILS	LARGE LYMPHOCYTES	SMALL LYMPHOCYTES	TYPICAL MONOCYTES	ATYPICAL MONOCYTES
	$\times 10^6$	%	$\times 10^3$	%	%	%	%	%	%	%
10-20	4.2	90	16.9	40				30		30
10-20			14.6	53				45	2	
10-24	3.9	75	12.4	47				33		20
10-25	3.8	75	15.0	57			3	34	6	
10-26	3.5	70	14.0	70	3	1		10	5	11
10-28	4.2	75	12.2	62	5		1	32		
10-28	4.3	83 (Sahli)	11.1	45	4	1		25	15	10
10-29	4.0	75	9.6	65	2		3	26	4	
10-30	4.1	80	11.6	63	3		7	27		
10-31	4.5	80	12.8	59	1	1	14	25		
11-1	3.5	70	11.8	53	2	2		39	4	
11-2	4.2	75	8.9	59			12	26	3	
11-4	4.5	80	9.0	66			6	26	2	
11-5			10.0	67	4		4	22	3	
11-6	4.3		8.3	49	4	1		40	6	
11-7			6.6	57	4		4	33	2	
11-8			7.8	58		2	7	26	7	
11-9			8.0	61	3		8	23	5	
11-10		75	10.2	62	2		7	24	5	
12-2	4.3	92 (Sahli)	8.9	66	2			29	3	

The blood Hinton, Wassermann and Widal reactions and the agglutination test for undulant fever were negative. Urinalyses were negative. Throat smears showed organism typical of Vincent's angina.

The pathological report by Dr. Shields Warren was as follows:

> The spleen with partly stripped capsule measures 18 by 12 by 6 cm. and weighs 660 gm. The capsule has been almost entirely stripped from one side, and reveals clotted blood forming a layer about 0.5 cm. thick covering almost all this side. The other side of the spleen is covered by very slightly wrinkled, but otherwise smooth, shiny membrane. Section shows the spleen to be partly fixed. From the central portion, which is very soft, a moderate amount of pulp can be scraped. A few small hemorrhagic foci can be seen within the fixed tissue near the periphery. Microscopically the normal structure of the spleen is well preserved. The trabeculae are not enlarged. The follicles are distinct, are of the usual size and present no inflammation or hyalinization. The sinusoidal structure is less prominent than normal, owing to the large number of cells filling the sinuses. There is a relatively small amount of blood in the pulp. A diffuse distribution of powdery granules of hemosiderin is present. The pigment is found in the endothelial cells of the sinuses and in free phagocytic cells in the sinusoidal spaces. The cells filling the sinuses are free endothelial cells, which are most numerous, large and small lymphocytes, plasma cells, polymorphonuclear leukocytes, and a few undifferentiated cells suggesting myelocytes. Mitotic figures are rare. One portion of the spleen shows an area of unorganized hemorrhage. The microscopic picture is compatible with infectious mononucleosis.
>
> Microscopic examination of the appendix shows es-

sentially the picture of healed appendicitis. The serosal lymphatics contain a few clusters of lymphocytes. There are scattered lymphocytes, chiefly perivascular, in the muscularis. There is also a slight degree of fibrosis in the inner portion of the muscularis and the submucosa. The secondary nodules of the lymphoid tissue of the submucosa are sharply demarcated, and contain cells that are large, with rather vesicular nuclei. Mitotic figures occur, but they are no more numerous than one frequently finds. Some of the cells are less clearly defined than usual. The mucosa itself is essentially negative. There is nothing distinctive in the appendix that would associate it with infectious mononucleosis.

Infectious mononucleosis is by no means a rare disease, and if the condition is kept in mind, there should be no difficulty in recognizing it. The cardinal symptoms are fever, headache, sore throat, generalized malaise and tender, enlarged lymph nodes, regional or general. The spleen is usually palpable. The blood picture, although not pathognomonic, is highly suggestive. One always finds an increased percentage of large atypical lymphocytes, with a corresponding decrease in neutrophils. The cells may suggest those seen in acute leukemias, and similar cells may be seen in infectious jaundice. In infectious mononucleosis there is very rarely anemia, and no reduction in the number of blood platelets, in contrast to that practically always found in acute leukemia. Usually in infectious mononucleosis there is a leukocytosis, but it should be kept in mind that a small percentage of cases have a definite leukopenia. Furthermore, in differentiating this condition from infectious jaundice, one must remember that icterus occurs in infectious mononucleosis in a certain percentage of cases. Lymphadenopathy, however, always precedes the icterus, so that the two conditions may be easily distinguished. The sheep-cell agglutination reaction, which becomes positive in infectious mononucleosis after about the tenth day of the disease, makes the diagnosis certain.

Although rupture of the spleen in this disease is very rare, its occurrence is serious enough to demand that infectious mononucleosis be treated with respect, and not on an ambulatory basis.

Summary

A case of rupture of the spleen in the course of infectious mononucleosis is reported, together with the detailed pathological report of the spleen.

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Reference

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MEDICAL PROGRESS

THE CAUSES AND TREATMENT OF EDEMA*

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EDEMA is an abnormal collection of fluid in tissue spaces. This may be a very localized phenomenon, or it may be generalized throughout the body. Few physical signs lend themselves so well as edema to physiologic analysis and interpretation and therefore it is not only frequently possible but highly desirable to understand the mechanism of edema production in any given case, so that the underlying cause can be specifically attacked and treatment can be made genuinely effective. There is a constant exchange of water and electrolytes and certain nonelectrolytes between the blood stream and the tissue spaces through the capillary walls. This interchange is kept in balance and the amount of tissue fluid is kept constant by two opposing pressures. The hydrostatic pressure within the capillaries tends to drive fluid out of the capillaries, whereas the osmotic pressure exerted within the capillaries, largely by the plasma proteins to which the capillary walls are normally nearly impermeable, tends to draw it back. Therefore, if either the hydrostatic capillary pressure is increased or the plasma colloid osmotic pressure is diminished, a condition favoring the development of edema results. A factor of importance not generally appreciated is the pressure exerted by the elastic subcutaneous tissues.[1] This tends to limit the amount of edema that forms in any given case, and also is in part responsible for the location of the edema — that is, other things being equal, edema fluid collects where the skin and subcutaneous tissues are relatively lax, as in the periorbital region. Under certain circum-

All articles in this series will be published in book form; the current volume is *Medical Progress: An annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

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stances, protein escapes through the capillaries into the tissue spaces, or is laid down in abnormally great amounts, thus raising the colloid osmotic pressure within the tissues. A more accurate expression, therefore, of the balancing of the opposing pressures between capillaries and tissue spaces would be: hydrostatic blood pressure in capillaries plus tissue osmotic pressure equals subcutaneous tissue pressure plus plasma osmotic pressure; normally, the hydrostatic blood pressure and the plasma colloid osmotic pressure are the important factors involved.

In addition, the total electrolytic concentration of body fluids is significantly concerned with the water balance of the body. The organism attempts to maintain the composition of these fluids constant, even at the expense of gain or loss of water itself. Hence anything that seriously affects the electrolyte balance of the body, so that sodium or chloride is retained, may under certain conditions lead to edema. Excellent discussions of this problem are presented by Gamble[2] and by Peters.[3] Many of the factors affecting electrolyte and water balance are still unknown, but knowledge of the role of the endocrine glands in this regard is increasing.

Causes of Edema

Increased Capillary Permeability

Toxic states — such as those from burns, bites, heat and cold, allergy, as manifested by urticaria or angioneurotic edema, and inflammation, as in cellulitis — all produce edema because of increased capillary permeability to protein and the local escape of fluid high in protein content into the tissue spaces, with a resultant increase in tissue colloid osmotic pressure. In some of these types of edema, the local release of a toxic substance, possibly histamine,[4, 5] may be responsible. This has led to the clinical attempt to "desensitize" persons who are subject to urticarial disturbances from exposure to cold, serum sickness, insulin hypersensitiveness and so forth, as well as certain types of headaches, by administering graded small doses of histamine[6–8] and by attempts to neutralize the histamine by giving histaminase,[7–10] a histamine-destroying enzyme found in the gastrointestinal mucosa. As yet clinical reports of the use of histamine have not been convincing enough to establish its value in this regard unequivocally, and the use of histaminase rests on no good physiologic foundation.[11]

Generalized edema occurs in the early stages of acute glomerular nephritis. It is now believed by most authorities that the edema is a result of the widespread capillary damage that occurs in this condition, with increase in capillary permeability.

Increased Hydrostatic Intravascular Pressure

Venous backpressure. Venous thrombosis or varicose veins are the commonest cause of unilateral or unequal edema of the lower extremities. Obstruction to the superior vena cava not uncommonly occurs with disease involving the superior mediastinum, such as aneurysm or tumor, and gives rise to a characteristic clinical syndrome. Inferior vena-cava obstruction is much rarer but also results in a typical picture. Portal-vein obstruction, of course, characteristically leads to ascites. When dependent edema occurs, it tends to develop late and is due in part to the pressure of the ascitic fluid on the vena cava, and in part to the hypoproteinemia, which is generally present.

When the venous pressure is *generally* raised, it almost always means congestive heart failure of the right-sided type. In addition to edema, distention of the peripheral veins is usually found, with jugular veins that remain engorged even in the semirecumbent position, and an enlarged tender liver. The only exception to heart failure as the cause of such a generalized increase in venous pressure is cardiac tamponade, which may be produced by fluid in sufficient quantity in the pericardial sac, or a constricting pericarditis.

Arteriolar dilatation. When arterioles become widely dilated, blood pressure within the capillaries increases and a condition favoring edema formation exists. This may occur regionally in connection with nerve injuries, since involvement of somatic nerves may be accompanied by vasomotor paralysis, although vasomotor spasm is of more frequent occurrence under these circumstances. Vasomotor paresis may also be of central origin. For example, it has been shown that hemiplegia of cerebral origin is usually accompanied by diminished vasomotor tone on the affected side,[12] and edema of moderate degree is not uncommon over this area.

It is possible that one of the factors involved in the generalized edema that may occur in beriberi is peripheral vasodilatation due to involvement of the vasomotor system.[13] Since, in this condition, heart failure may also occur, there may exist edema and a high venous pressure at a time when the circulation time is normal or shortened, a combination of events that is most unusual and is found in only two other types of congestive heart failure: that caused by hyperthyroidism and that secondary to arteriovenous aneurysm.

Lymphatic Obstruction

Chronic obstruction of the lymphatics draining an extremity gives rise to edema that is difficult to distinguish from that consequent on venous obstruction. It tends to be rather more brawny in character, and there is no color or temperature change. One remarkable tendency manifested by patients with such edema is the frequent development of superficial infections of the involved extremity, resembling lymphangitis or cellulitis.

Edema from lymphatic obstruction is not very rare. Although filariasis is unknown in this section of the country, and neoplastic lymphatic obstruction is usually dramatic and well recognized, a not very uncommon, but usually unrecognized, cause of edema of one or both legs is lymphatic obstruction due to pelvic inflammatory disease, which may have been inactive for years. Since such disease is also prone to lead to deep thrombophlebitis, the differentiation of the cause of the resulting edema may be difficult or impossible. An uncommon but interesting type of lymphedema is that known as Milroy's or Meige's disease,[11] a familial affection of unknown etiology, involving one or both lower extremities.

Hypoproteinemia

Hypoproteinemia may occur as the result of deficient protein intake, of increased protein loss or of impaired formation of the plasma proteins. Severe grades of malnutrition in persons whose diets are unusually deficient in protein may lead to edema. In certain disturbances of the gastrointestinal tract (sprue, diarrhea and the changes due to massive resections and to the congestion of heart failure), the absorption of many vital food substances may be impaired, and in some cases the absorption and utilization of protein itself are interfered with. Many patients of this type who show hypoproteinemia have either deficient diets or disturbances of liver function as important causative factors.

Not uncommonly, a deficiency in protein intake is a contributory cause of an edema the major etiology of which is traceable to some other disease, for example, cardiac edema.[15]

Another important cause of hypoproteinemia is, of course, loss of plasma protein, and the commonest and most important channels through which this is lost are the kidneys. Edema resulting from this cause is known as "nephrotic edema" and is seen in the nephrotic stage of glomerular nephritis, in "lipoid nephrosis" and in amyloid disease. The correlation between clinical findings, physiology and pathology has been especially imperfect in this condition. It is generally accepted that protein is chiefly excreted through the glomeruli, and yet it is frequently difficult to demonstrate clear-cut pathologic changes in the glomeruli, although recently by special staining methods glomerular lesions have been shown to occur in most cases of nephrosis. A controversy has long raged about whether lipoid nephrosis is a specific disease entity or a stage of glomerular nephritis, and if a specific disease, whether a primary renal disturbance or metabolic disorder, as contended by Epstein. It is not relevant to the subject at hand to enter into this controversy, except to mention that there has recently been reported a good deal of work bringing forward evidence of various sorts that the plasma and urinary proteins in nephrosis and even in the nephrotic stage of nephritis may be qualitatively different from normal plasma proteins.[16–20] Whether this difference is primary and possibly a cause of the proteinuria, or whether it is merely the result of the prolonged drain of chronic protein loss on protein formation is not yet established.

Other less common channels by which blood proteins may be lost, which may under certain circumstances be very important, are serous effusions, such as ascites, burned surfaces and, especially, hemorrhage, acute or chronic.

The factor in the causation of decreased plasma proteins that has received attention most recently is deficient protein formation. Although the sites of formation of all plasma proteins are not conclusively established, it is probable that the liver is specifically concerned, undoubtedly with fibrinogen and probably with albumin synthesis, and it is known that disease of the liver is frequently accompanied by hypoproteinemia.[21, 22] Lowering of the plasma proteins is frequently considered a clinical test of poor liver function. Hypoproteinemia is usually found in advanced portal cirrhosis and is often a chief contributing factor in the ascites and edema found in this condition.

Low plasma proteins are not uncommonly present in patients with congestive heart failure. There are several possible factors involved. One, already mentioned, is the deficient protein intake of many of these patients. A second is protein loss through the kidneys and, to a lesser extent, in pleural and peritoneal effusions. A third is impaired protein formation, probably due to depression of liver function consequent on the hepatic congestion and anoxia. Another cause of the lowering of the protein concentration in the plasma is dilution of the blood, owing to hydremia, especially in patients in whom diuresis has or is about to set in.[23]

Disturbances of Electrolyte and Water Balance

The composition of tissue fluid is kept extraordinarily constant, and even when it collects in

abnormal amounts, the change is quantitative rather than qualitative, since its composition remains essentially unaltered. The chief base or cation concerned is sodium, which makes up about 140 of the total of 150 milliequivalents per liter. Anything that tends to increase the total amount of sodium in the body favors the production of edema, and conversely anything that depletes the total body sodium leads to dehydration. It is difficult for a normal person to change his body sodium materially because of the immediate and accurate adjustment the kidney is able to effect, but in any condition already present that predisposes to edema, it may be then possible to lessen the sodium present in the body, and hence the amount of edema, by withholding salt from the diet or by facilitating its excretion, as by the administration of an acid-producing salt, such as ammonium chloride or nitrate.

The role of the endocrine glands in electrolyte and water balance is being increasingly studied. Interestingly enough, many of the hormones of the endocrines that have been investigated have been found to lead to retention of sodium and chloride and hence of water, thyroxin being the major exception. Perhaps the most striking in this respect is the adrenocortical hormone. It is well known that a deficiency of this substance, as in Addison's disease, leads to sodium loss, rise of blood potassium, dehydration and shock. Administration of this hormone and of the synthetic desoxycorticosterone to normal and adrenalectomized animals, and to human patients with Addison's disease, causes sodium and water retention,[24] and cases have been reported in which the giving of desoxycorticosterone in therapeutic doses to patients with Addison's disease has resulted in generalized edema and even in hypertension, hypervolemia, pulmonary edema and heart failure.[25, 26] It is possible that the hypertension and edema of Cushing's syndrome is associated with an excess secretion of adrenocortical hormone.[27]

Most of the hormones of the ovary and testis (estrone, progesterone and testosterone) have been shown to produce salt and water retention.[28] An interesting clinical state is cyclic menstrual edema.[28–31] This rare condition is apparently an aggravation of a normal physiologic change in which many women retain significant amounts of water during the periods of maximal estrone secretion, that is, at the time of ovulation and even more during the days just preceding menstruation. The treatment of cyclic menstrual edema is not very satisfactory, although in individual cases success has been reported from the administration of the anterior-pituitary-like hormone obtained from the urine of pregnant mares and from the use of Emmenin (an estrone-containing preparation), as well as ammonium chloride and a low salt diet.[31]

During pregnancy, the majority of women retain water, and in a considerable percentage edema actually results. When such women in addition suffer from hypoproteinemia due to protein malnutrition or ingest an excess of salt, edema is especially likely to occur, and according to Strauss,[32] in a certain number the clinical picture of preeclamptic toxemia develops. Weiss et al.[33] are of the belief that toxemia of pregnancy necessitates the presence of some unknown factor, apparently elaborated in the placenta.

It has been known for a long time that lesions of the posterior portion of the pituitary gland or some adjacent structure in the hypothalamus may lead to diabetes insipidus or polyuria due to failure of tubular re-absorption of water. The exact location of the lesion producing these conditions has been in dispute, some contending that it is in the base of the brain and others that the neurohypophysis is responsible. Dandy's[34] report demonstrates that when the posterior portion of the pituitary gland is deprived of its nerve supply through section of its stalk, diabetes insipidus may result. Extract of the posterior pituitary gland (pituitrin) or more specifically its pressor fraction, Pitressin, counteracts this disturbance, and its antidiuretic effect resides in its power to promote renal tubular reabsorption of water.[35, 36] It is also known that diabetes insipidus does not occur in the absence of the anterior portion of the pituitary gland, and there is evidence[37] that anterior-pituitary extract exerts a diuretic effect. It can be said, therefore, that normally the posterior portion of the pituitary gland exerts an antidiuretic and the anterior portion a diuretic effect, and that these opposing actions are in equilibrium.

Lack of thyroid hormone, as clinically seen in myxedema, gives rise to retention of tissue fluid high in protein content. As shown by Byrom,[38] this is due to an increase in the mucoprotein of the intercellular regions, the architectural skeleton that holds the cells together. As a result of this increase in protein in tissue fluid, its colloid osmotic pressure is increased, salt and water are retained and edema or more properly myxedema may result. The edema of hypothyroidism is thus of a unique type.

The administration of thyroid extract, or the clinical condition of hyperthyroidism, leads to the opposite effect: loss of interstitial protein, fluid and dehydration.

The effect of insulin in promoting water retention has been the occasion of a good deal of investigation and speculation. It is well known that

following the institution of insulin therapy in diabetic patients prompt gain of weight may occur, much of which is due to water retention.[39] This is apparently because the storage of glycogen is accompanied by water retention, whereas when fat metabolism predominates water is lost.

Clinical cases of edema following insulin administration have occasionally been reported. The causation of the edema is probably diverse. Rarely hypersensitivity to insulin, especially to protamine insulin, develops, with resulting urticaria or angioneurotic edema.[39] The edema that has been reported following diabetic coma and acidosis may well be due to the hypoproteinemia that frequently occurs. There is no evidence that insulin exerts any significant effect on sodium or chloride metabolism.[40]

Hence, the endocrine glands undoubtedly play an important role in electrolyte and water balance. Most of them operate through their effect on sodium or chloride or protein retention. Posterior-pituitary extract is unique in that it apparently causes specific retention of water itself through its effect on the renal tubules. In the light of present knowledge, however, it cannot be said that endocrine disturbances are a frequent cause of marked clinical edema, or that therapy with hormonal preparations is often of value in the treatment of edematous states.

When edema occurs in patients with vitamin deficiencies the usual cause is hypoproteinemia due to protein malnutrition. Another type is the edema seen in beriberi, which has already been discussed. This may in part be due to congestive heart failure secondary to the effect of the deficiency on the heart itself, and in part to peripheral vasodilatation caused by vasomotor paresis. The present evidence indicates that this particular disturbance is largely or entirely the result of lack of vitamin B_1 and is relieved by the administration of thiamin. There may occur, however, edema in patients with deficiency of the vitamin B complex, which is not relieved by thiamin or by riboflavin but is cured by the giving of whole yeast.[41] In other words, this edema, of undetermined nature, is due to the lack of an unidentified substance present in yeast. There is no evidence that lack of the other vitamins is a factor in the formation of edema.

Edema occurs not uncommonly in severely anemic patients, and this symptom, together with the breathlessness such patients usually manifest, has frequently led to the mistaken diagnosis of heart disease or heart failure as the primary cause of the clinical picture. It is true that anemia may precipitate heart failure in a patient with underlying heart disease, but edema as usually seen in patients with anemia is of a different origin. Sometimes it is caused by hypoproteinemia, owing to an associated protein deficiency; often, however, the edema seen in anemia is explained by none of these causes.[42] The severity of this is in general in proportion to the degree of anemia, and is aggravated by the administration of sodium salts. Occasionally, however, patients with untreated pernicious anemia fail to exhibit edema until after the institution of therapy and the beginning of improvement. The cause of this type of edema is still obscure.

Technical Clinical Methods for Evaluation of Edema

The etiology of edema can usually be determined by a careful history, a physical examination and a routine urinalysis. Occasionally, however, further laboratory assistance must be called for. The most useful of these tests, and one that should be easily available, is determination of the plasma or serum proteins. These normally vary from about 6 to 8 gm. per 100 cc. It has been shown that, as they become diminished, water accumulation in the tissues increases because of the lowered plasma osmotic pressure, and when they reach a level as low as 5.0 to 5.5 gm., this fluid retention is usually manifest as edema.[43] A more accurate gauge than the total plasma proteins is the determination of the levels of the albumin and globulin separately. Normally, albumin makes up about 60 per cent of the total protein, and globulin 40 per cent. Any lowering of the plasma proteins is mainly at the expense of the albumin fraction, which, having the smaller molecule, is more easily lost through the capillary or glomerular walls but also for the same reason has a greater effect on osmotic pressure. A lowering of the plasma albumin from its normal of about 5.0 gm. to 2.5 gm. or below is likely to result in edema.

A simple and highly accurate estimate of the total plasma proteins can be reached by determining the plasma or serum specific gravity, which varies in direct proportion to the protein.[43] There are now available several ingenious methods by which the plasma specific gravity can be quickly and accurately determined.[44–46] These, in the main, depend on the speed of fall of a drop of plasma or serum through a liquid of known density with which it is immiscible, or the insertion of such a drop into a liquid with a differential density varying from light to heavy and determining the level in the liquid the drop attains. Since the determination of hypoproteinemia is so frequently of value, it is to be anticipated that the estimation of plasma proteins will soon come to be a routine laboratory procedure that in clinical usefulness will

rank with nonprotein-nitrogen and blood-sugar determinations.

The direct measurement of venous pressure can be carried out quickly and easily by the insertion of a needle (18 to 19 gauge) into an antecubital vein, connecting it with a manometer filled with saline, and relating the height of the saline column to the estimated level of the right auricle.[47, 48] This normally is either 10 or 15 cm. of water or less, depending on whether the reference point is the front or back of the chest.

In most cases of congestive heart failure, this procedure is unnecessary, since the cause of the edema is evident and an estimate of the venous pressure can be made by determining the height to which the jugular veins remain filled with the patient in the sitting or semireclining position. However, there are times when one cannot be sure whether edema of the lower extremities is due to local venous obstruction or the generally increased venous pressure of cardiac failure, in which the findings of an elevated venous pressure in the arm will answer the question. Moreover, by measuring the venous pressure in two places, as for example in each arm or in an arm and a femoral vein, venous obstruction sometimes can be diagnosed and localized.

Estimations of the various blood electrolytes are of greater value in states of dehydration than in edematous conditions, since, as already stated, in edema they may be quantitatively normal.

Treatment of Edema

The treatment of edema, like that of most other pathologic states, resolves itself into an attempt to attack the underlying cause directly, and into nonspecific measures.

Nothing need be said here about the specific treatment of localized allergic or inflammatory edema, of that resulting from venous obstruction, or of the edema of congestive heart failure.

The logical way of treating edema due to hypoproteinemia is, of course, to raise the plasma proteins. When these are low because of diminished intake they can be easily increased by giving a diet adequate in protein. When the difficulty is caused by increased loss, results from high-protein feeding are less satisfactory but still the most logical procedure. If liver disease is responsible for impaired production, the value of feeding excessive protein is problematical.

Recently, experimental work has been reported regarding the intravenous administration of amino-acids for the purpose of maintaining protein balance and of raising low plasma-protein levels.[49–51] The results are interesting and suggestive but still in the experimental stage, and more investigation is needed before the clinical value and safety of this procedure can be considered proved.

A successful way of temporarily raising plasma proteins is by the actual administration intravenously of the proteins themselves. For a long time this could be accomplished only by whole-blood transfusion and this is still the procedure of choice if anemia exists. But if there is no deficiency in red cells, plasma transfusions, which are now in use and becoming increasingly available, are to be preferred, and the various methods for obtaining highly concentrated plasma solutions are rapidly being improved to a point where they will be widely applicable and the side reactions will be minimal.[52, 53]

For many years, it has been advocated that a substitute colloid be administered that will be nontoxic and will have the osmotic effect of plasma proteins. Acacia appeared to fulfill these requirements, and has been and is extensively employed. A few years ago, the use of acacia was largely abandoned, chiefly because of the many bad results reported, some of which were undoubtedly due to improperly purified and prepared acacia solutions. It was also believed that the repeated administration of acacia to a patient could in the long run be deleterious, since it might act by further depressing the plasma-protein level. Recently, several reports from the Mayo Clinic[54] and elsewhere of the use of acacia with excellent results have revived interest in this substance, and further investigation of its value now seems warranted.

The first of the nonspecific measures to be attempted in the treatment of any widespread edema is the exclusion of sodium chloride and other sodium-containing salts from the diet, and possibly the attempt at increasing sodium excretion by the administration of an acid-producing salt, such as ammonium chloride (6 to 10 gm. daily).

Urea in oral doses of 45 to 90 gm. a day is also sometimes effective. Intravenously administered hypertonic solutions, such as glucose, sucrose, sorbitol and magnesium sulfate, may produce a diuresis, although a temporary one at best. These substances, in particular magnesium sulfate, are especially of value in conditions in which there are cerebral symptoms associated with cerebral edema. It should be remembered that all hypertonic solutions, if given rapidly in fairly large amounts, temporarily increase blood volume and hence act as a strain on a weakened heart, and also that the late effect of glucose may be exactly the reverse of that desired, that is, water retention with increase of edema may occur. More-

over, it has been reported that intravenous sucrose may cause renal damage.[55]

Of the drugs used as diuretics the most popular at present, and deservedly so, are the mercurials, of which merbaphen (Novasurol), mersalyl (Salyrgan) and Mercupurin are the best known. These should be given intravenously if possible, are tolerated intramuscularly, but cannot be administered subcutaneously. They are practically nontoxic. A rare case of intolerance to them may occur. I have seen but one case of renal irritation out of a great many thousand injections. If effective in a patient, they can be given repeatedly without harm. Many patients have had hundreds of injections over a period of years, at weekly or semi-weekly intervals. The dose is 1 to 2 cc.; larger doses are usually inadvisable. The exact mode of action of these drugs is still in dispute. A recent report[56] suggests that under certain circumstances the blood volume may be considerably increased prior to diuresis, and these authors therefore suggest, to avoid the possibility of undue strain on the heart, the administration of smaller doses (0.5 cc.) thrice daily.

The inconvenience of the intravenous injection of the mercurial diuretics has led to an attempt to find other routes of administration. Suppositories containing the drugs are available but, although often effective, have not proved entirely satisfactory because of the rectal irritation that often results. A recent report[57] of an effective oral preparation is promising, but further work is required before its value can be considered established.

Although the mercurial diuretics are on the whole the most effective and have received especial attention in the last few years, the xanthine group should not be forgotten. Although theophylline itself is the most potent of the xanthine group, its tendency to produce nausea has led to its use mainly in combination with other salts, such as theophylline sodium acetate, 5 to 10 gr. thrice daily, and theophylline ethylene diamine (Aminophylline), 1½ to 3 gr. thrice daily. The latter, however, is of greater clinical value when used as a bronchial dilator or vasodilator than as a diuretic. Theobromine, usually administered in combination with sodium salicylate (Diuretin), 40 to 60 gr. daily, is mild but well tolerated. More effective is theobromine calcium salicylate (Theocalcin), 20 to 40 gr. daily.

Summary

A scheme has been presented for the evaluation of clinical edema in accordance with the underlying disturbance involved; the various causes of edema and of certain disturbances of the electrolyte and water balance have been discussed; certain technical aids in the assessing of the nature of the edema have been considered; and its treatment has been described.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27251*

PRESENTATION OF CASE

A two-year-and-nine-month-old boy was well until two months before entry, when he contracted what was considered to be pertussis. At the same time the siblings were said to have suffered from pertussis. For the first three weeks of his illness he was up and about, had a good appetite, but lost weight, and for the last month was so ill that he had to remain in bed. His temperature rose to 102°F. daily. Paroxysms of coughing continued, but the whoop disappeared. For the three days before entry, the cough was much worse, and hospitalization was advised.

The family and past histories were irrelevant.

Physical examination revealed an extremely emaciated boy without any subcutaneous fat and with marked loss of muscular tissue. He was quite pale and ill, with a severe, loose cough, producing moderate amounts of very foul purulent sputum without blood. He was dyspneic and slightly cyanotic. His skin was dry and rough, and there was a slight hyperkeratosis about the hair follicles. The eyes were normal; the ears and nose were normal. The abdomen was distended and tympanitic. The liver and spleen could not be felt. There was no tenderness or spasm. There was definite clubbing of the fingers and toes. There was a pronounced Harrison's groove, but no great enlargement of the costochondral junction. The heart was normal. The right lung was hyper-resonant, and breathing was greatly exaggerated. There were numerous loud adventitious sounds referred from the opposite side; there were no fine rales on the right. The left chest was dull to flat throughout, particularly over the left base and in the axilla. Breath sounds were diminished and replaced by numerous loud rales, rhonchi and bubbling sounds. Tactile and vocal fremitus were increased over the areas of dullness. There was amphoric breathing in the area of flatness in the left lower axilla.

The urine was normal. The blood showed a moderate secondary anemia, no leukocytosis and a normal differential count. A 1:1000 tuberculin test was negative. Type 23 pneumococcus was isolated from the throat.

X-ray films of the chest revealed complete opacity on the left, with a suggestion of cavitation at the left base. The right lung showed a diffuse fine mottling consistent with, but not diagnostic of, tuberculosis. X-ray films of the long bones revealed osteoporosis.

From entry the patient was desperately ill, the fever remaining between 101 and 103°F. The cough was extremely severe, producing large amounts of foul sputum. Repeated examinations of the sputum for acid-fast bacilli were negative. The patient was given the usual supportive treatment, including two small transfusions of citrated blood and a transfusion of blood serum. He was placed in an oxygen tent the last few days of life. The patient's condition was too precarious to allow any further diagnostic or therapeutic measures, and he died six days after entry.

DIFFERENTIAL DIAGNOSIS

DR. DONALD KING: I have not yet seen the x-ray films, but wish to give you my preliminary reactions on reading the summary of the case. There are four points I shall make.

In the first place, it is obvious that the boy had a pulmonary abscess or multiple abscesses. In this clinic at the present time we are not using the term "gangrene of the lung," but I am sure that in many clinics a case like this, with high fever, very foul sputum, marked loss of weight and rapid progression to death, would be so classified.

My next point is concerned with the etiologic organism of this abscess. We are told that Type 23 pneumococcus was isolated from the throat and that no tubercle bacilli were found, but we are given no further bacteriologic data. I do not believe that Type 23 pneumococcus would give the abscess and foul sputum, and we have no reason to believe that a Friedländer bacillus or yeast or other fungus was present; hence we must assume, I believe, that the pulmonary abscess was caused by the group of anaerobic mouth organisms, including spirochetes, fusiform bacilli, vibrios and cocci. Just how these organisms found their way into this patient's lung and set up the infection is not clear.

Thirdly, what about the relation of whooping cough to lung abscess? We must assume that the boy had whooping cough, because he and his brothers and sister whooped. But lung abscess is a very rare complication of this infection. There is no mention of it in the literature, and in our series of 212 cases of pulmonary abscess, none were associated with pertussis. Of course, in bron-

*This case is presented through the courtesy of the Children's Hospital, Boston.

chiectasis the story is different. Whooping cough is frequently given as the cause of this disease, and in our series of 400 cases 9 per cent were said to have followed pertussis. Present opinion is that two factors are necessary for the production of bronchiectasis: bronchial obstruction, which may be partial or complete, and infection. It has been suggested that in whooping cough enlarged mediastinal lymph nodes are responsible for partial bronchial obstruction. I should like to get some help from the x-ray men and Dr. Farber regarding this point. The textbooks do not help. They talk about bronchitis and emphysema associated with whooping cough, but do not mention enlarged nodes.

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DR. JAMES R. LINGLEY: We see very few chest films of children with whooping cough. However, our impression is that inflammatory lymph nodes, unless tuberculous, are rarely seen by x-ray.

DR. KING: Then it is up to you, Dr. Farber. Do enlarged lymph nodes occur commonly with whooping cough, and is it possible that they give bronchial obstruction and therefore lead to bronchiectasis? And, in the case that we are considering, could enlarged nodes have been a possible factor in producing the pulmonary abscess?

DR. SIDNEY FARBER: I should think not, in a case of uncomplicated pertussis.

DR. KING: Then neither the roentgenologist nor the pathologist can give any support to this theory.

Finally, what other causes were there for the abscess? In any child of two years and nine months with an abscess or persistent lung disease, one wonders about the inhalation of a foreign body, and we must consider this possibility, although we have no evidence for it. Also we should think of congenital lung changes, possibly cystic, as a basis for later suppuration. There is again no evidence in this case. If this were an adult we should think of bronchial tumor, either benign or malignant, but such a diagnosis seems very unlikely in a child.

We now come to the interpretation of the x-ray films, and the points in which I am interested are, first, whether the heart was displaced toward the left, giving evidence of atelectasis, or toward the right, making one suspect the presence of a large amount of fluid in the left pleural space; and secondly, what we are to do about the shadows in the right lung, which are interpreted as "fine mottling consistent with, but not diagnostic of, tuberculosis."

DR. LINGLEY: The films show an extensive destructive process on the left side, with multiple cavities; the diaphragm is slightly elevated on the left, and there is a slight displacement of the heart to the left. The trachea likewise is a little displaced.

DR. KING: But no evidence of what one would consider real atelectasis or drowned lung, with bronchial obstruction?

DR. LINGLEY: The collapse must have been of slight degree.

DR. KING: Do you want to help as to the presence of fluid?

DR. LINGLEY: I think there is very little, if any, fluid.

DR. KING: Certainly the story and physical findings seem to be against fluid.

DR. LINGLEY: On the right side, there is mottling throughout the entire lung, a miliary process quite consistent with miliary tuberculosis.

DR. KING: Of course, I am "on the spot" with this miliary lesion. Here is a child with a negative tuberculin test, using a 1:1000 dilution, and repeated negative smears for tubercle bacilli in the sputum. In an adult I should think of sarcoid disease, miliary carcinoma and possibly silicosis or yeast or fungus infection. In this child, with such an x-ray film, it is difficult to make any other diagnosis than tuberculosis in the right lung. The negative tuberculin test could be explained because the child was moribund, and dying from overwhelming infection. If the tuberculous process were primarily hematogenous and the process in the lung had not yet gone on to cavity formation, the sputum might still have been negative. I do not believe that pulmonary suppuration on the left side spreading to the right would give this roentgenologic picture. Is that so, Dr. Lingley?

DR. LINGLEY: Yes.

DR. KING: Everything considered, I should make the diagnosis of multiple pulmonary abscesses and miliary tuberculosis.

DR. TRACY B. MALLORY: Are there any other suggestions or alternative diagnoses?

DR. HAROLD L. HIGGINS: I should think that the miliary process might come from plain bronchiectasis; it seems more or less localized.

DR. KING: It is diffuse from the top to the bottom of the right lung.

DR. MALLORY: Dr. Lingley, you do not know the answer; it may be fair to ask your opinion.

DR. LINGLEY: Tuberculosis is my diagnosis.

DR. KING: All tuberculosis?

DR. LINGLEY: Yes.

DR. KING: We have to have something more than tuberculosis to give foul sputum. I do not believe tuberculosis by itself would give that.

DR. LINGLEY: The patient probably had secondary infection, but the main process, I believe, was tuberculous.

DR. KING: If it was tuberculosis, the patient might have had tuberculous nodes that gave bronchial obstruction.

CLINICAL DIAGNOSES

Pertussis, convalescent.

Bronchopneumonia, secondary (Type 23 pneumococcus).

Lung abscess, left lower lobe.

Chronic malnutrition, with multiple vitamin deficiencies.

Tuberculosis?

DR. KING'S DIAGNOSES

Multiple pulmonary abscesses.

Miliary tuberculosis.

ANATOMICAL DIAGNOSES

Pulmonary tuberculosis, with cavitation, left lower lobe.

Miliary tuberculosis.

Lung abscess, left lower lobe.

Bacteremia, terminal (Type 23 pneumococcus).

Acute bronchopneumonia, right (Type 23 pneumococcus).

Vitamin A deficiency.

Pertussis, convalescent (clinical history).

PATHOLOGICAL DISCUSSION

DR. FARBER*: I had to go back to 1935 to find a case of tuberculosis that did not have the diagnosis of tuberculosis stamped all over it.

This patient did have tuberculosis, and there were certain other findings. The child was very much emaciated, a finding not characteristic of tuberculosis in early life. There was a peculiar dryness of the skin, which was remarked on in the history and which was considered by those clinicians who saw the patient to be suggestive of a deficiency disease, the exact type of which was not mentioned. At autopsy we found some evidence of vitamin A deficiency, as shown by metaplasia of the lining epithelium of the trachea and bronchi, although no change was present in the ducts of the pancreas or the renal pelves. The vitamin A levels, determined during life from the blood and at autopsy from the liver, were low.

In the lowermost portion of the left lung was an area of caseation, and the lymph glands on that side showed the classic spread of tuberculosis, the characteristic picture of the lymph-node component of the primary lesion. In the right lung the picture was much more that of miliary tuberculosis, but that was not all. Here we also found massive acute pneumonia caused by a Type 23 pneumococcus, the organism recovered from the heart's blood at the time of autopsy. A deeper cut showed the cavity on the left, which Dr. King discussed and which was a mass of necrosis and caseation. Almost the entire lower lobe on the left was involved in the process. Whether a foreign body had been there, or aspiration of food had occurred into a small area of tuberculous infection, I cannot say from the findings at autopsy; it is highly probable, however, that some such factor must have been added to the tuberculous process to produce this kind of lesion and the type of sputum described.

A minimal number of lesions were found in other parts of the body. There were miliary tubercles in the liver, kidney, spleen, bone marrow and many other organs of the body. This type of spread is a hematogenous one. One section of the lung shows an area in which the process is breaking into a bronchus by direct extension and destruction of the bronchial wall. Another shows a much more characteristic type of Ghon lesion, with a small area of consolidation just beneath the pleura, surrounded by satellite tubercles, and with spread to the regional lymph nodes. There was a tuberculoma of the cerebellum — a lesion rarely seen at the present time. Still another rare lesion at autopsy was massive mesenteric lymphadenitis caused by the tubercle bacillus.

I might add just one point concerning the relation of pertussis to a lesion of this kind. Pertussis may accelerate the tuberculous lesion that has existed previously, as is well known, or may be responsible for aspiration of vomitus, food or foreign bodies during paroxysms and thus bring about secondary damage to the lungs, quite apart from the initial pathologic process. In pertussis, the uncomplicated disease is a superficial one involving the cilia of the upper respiratory tract. The major symptom is brought about by the presence of the organisms in the cilia, with interference with ciliary activity. The lymph nodes at the hilum of the lung become involved only when complications due to secondary invaders occur.

A PHYSICIAN: Do the enlarged nodes narrow the bronchus?

DR. FARBER: No; not to any important degree, except in cases of chronic bronchopneumonia.

DR. KING: We really have three conditions here: — the abscess, the pneumococcal infection and the tuberculosis.

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CASE 27252

Presentation of Case

First Admission. A sixty-nine-year-old construction worker entered the hospital complaining of severe frontal headaches of five weeks' duration.

One week before entry, the headache shifted to the temporal regions; it included first the left and then the right, and was accompanied by a sore throat, a fever of 102°F. and redness and swelling of the face to the point where both eyes were closed. Furthermore, there was exquisite tenderness of the left scalp.

On examination the left face was swollen, and the left scalp acutely tender. There were cardiac enlargement, aortic regurgitation and a Corrigan pulse. The blood pressure was 180 systolic, 70 diastolic. A rectal examination was said to have been negative. The white-cell count was 12,800; the blood Hinton reaction was positive, the spinal-fluid Wassermann reaction negative.

Within a few days, the facial swelling subsided somewhat, and an unusual prominence of both superficial temporal arteries was noticed. Although pulsation was not visible, it was palpable, albeit somewhat reduced, and tenderness was present along the main trunks and branches. Pressure on the carotid arteries relieved the headache. The temperature was found to rise regularly in the afternoon. A biopsy specimen was taken from one of the arteries, and histologic examination disclosed temporal arteritis. Three weeks after admission, the patient's symptoms had subsided spontaneously and he was discharged.

Second Admission (two months later). In the interval the patient had felt perfectly well except for slight constipation, which had been relieved by laxatives. Two days before admission, he noticed anorexia and began to pass large amounts of gas by mouth and rectum. Nothing further occurred until a few hours before entry and half an hour after a rather small, loose, bowel movement. At the time, the patient was bending over and was seized with a constant, sharp, crampy hypogastric pain accompanied by profound weakness and the passage of more gas by mouth and rectum. He lay down and applied a hot-water bottle to his abdomen, with some relief, but an hour later suffered a shaking chill, followed by fever and sweating. The patient's physician was called and recorded a temperature of 102.7°F. and soreness in the left lower quadrant; he advised immediate hospitalization. At the time of admission, the pain was more intense, arising in waves every five to ten minutes and breaking within twenty seconds; it seemed to originate in the left lower quadrant, shifting to the umbilical region and right lower quadrant. Each time an attack occurred the patient had a desire to move his bowels and complained that it hurt to shift his legs. He denied nausea, vomiting and dizziness and said that he had gained weight since his last illness, when he had lost 40 pounds.

The additional physical findings were as follows: The patient appeared acutely ill. The blood pressure was 100 systolic, 40 diastolic. In the distended abdomen there was diffuse tenderness, most marked in the lower portion, and spasm was noted in the left lower quadrant. Peristalsis was hypoactive except during the attacks of pain. On rectal examination, a 3-cm. to 4-cm. cauliflower-like mass was palpable on the right anterior wall of the rectum, 9 cm. from the anal orifice; its surface bled freely.

The temperature was 102°F., the pulse 89, and the respirations 20.

The urine showed a + test for albumin. The blood showed a red-cell count of 4,600,000 with a hemoglobin of 75 per cent, and a white-cell count of 20,000. The nonprotein nitrogen of the blood serum was 29 mg. and the protein 6.5 gm. per 100 cc.; the chlorides were 105.2 milliequiv. and the carbon dioxide combining power 25.7 milliequiv. per liter. The stools were liquid, thick and gray black, and gave a ++++ guaiac reaction.

A flat abdominal x-ray film showed dilated, air-filled loops of small intestine, particularly on the left side. The colon was moderately dilated. A film of the chest taken with a portable machine was negative.

The patient was given a 500-cc. blood transfusion, and a Miller–Abbott tube was passed. During the next nine days he improved tremendously; feces and flatus passed per rectum, the abdominal distention subsided, the white-cell count dropped to 12,000, and the temperature fell. Gradually a tender mass, definitely not the one felt rectally, localized in the left lower quadrant. A proctoscopic examination two weeks after admission revealed a hard, movable, ulcerated lesion on the anterior rectal wall, 12 cm. from the anus. A biopsy of the mass showed adenocarcinoma, Grade II. Twelve days later an operation was performed.

Differential Diagnosis

Dr. John D. Stewart: May we see the x-ray films?

Dr. George W. Holmes: The films of the chest show no evidence of metastasis to the lungs. They do show enlargement of the left side of the heart, with some tortuosity of the aorta. The position of the diaphragm is normal. This film was taken

to determine whether there was free air in the abdominal cavity, and there is no evidence of it. The next film shows moderately dilated loops of small bowel in the left upper quadrant, a rather characteristic picture of gas-filled, moderately dilated loops of jejunum. I do not want you to put too much weight on that statement. It may be ileum, but I think it is jejunum. Then, after the passage of the Miller–Abbott tube, the films show deflation and the disappearance of a large amount of gas in the intestinal tract. I do not see any evidence pointing to the nature of the obstruction.

DR. STEWART: It seems clear to me at the outset that this patient's abdominal pain was intestinal colic, and other causes of abdominal pain can therefore be passed over. Furthermore, it seems clear that the intestinal colic was due to obstruction and not to other causes such as enterocolitis or food poisoning.

The causes of acute intestinal obstruction may be divided into three general groups, the neurogenic, the mechanical and the vascular. In this case, the neurogenic causes can be eliminated at once, in my opinion, because of the severe crampy abdominal pains, the bloody diarrhea and the development of spasm and tenderness in the left lower quadrant. Then, if the obstruction was either mechanical or vascular in origin, did strangulation enter the picture? The manifestations of acute mechanical intestinal obstruction vary, depending on the extent of interference with the blood supply to the bowel. There is some reason in this particular case to suspect strangulation: the decline in blood pressure, the rapid onset of severe pain, the development of localized tenderness and spasm and, subsequently, the development of a mass in the left lower quadrant, all of which are consistent with a process interfering with the blood supply to the bowel. However, the same findings also fit with an interference with bowel function coming from a primary vascular accident. As Dr. Holmes pointed out, there are dilated loops of small intestine. There is also gas in the large intestine. That, to my mind, — since this patient was not given an enema, in which way air may be injected into the colon, — suggests an incomplete obstruction to the lumen of the bowel, probably in the small intestine rather than in the large. I might say at this point that I do not believe that the carcinoma of the rectum, which the patient had, contributed to the symptoms that brought him into the hospital at the second admission. If we conclude that there is evidence of strangulation and of incomplete obstruction to the lumen of the bowel, a fair diagnosis to make is a primary vascular accident of some sort, either embolic or thrombotic. As to what the primary lesion was in the vascular system we can only speculate. There was a possible source of emboli in the aortic lesion that this man had, and perhaps in the arteriosclerotic lesions that he probably had.

At this point we turn to a consideration of the episode that brought him into the hospital the first time. This was apparently a very bizarre picture, the exact nature of which I cannot make out. There were protracted headache and an illness associated with the loss of 40 pounds in weight; the culminating symptoms were fever, sore throat and swelling of the face, the description of which sounds like a cellulitis of the face; there was spontaneous subsidence of the evidence of infection and localization of the process in the temporal arteries, and the diagnosis of temporal arteritis was made by biopsy. Whether the general infectious process involving the arteries was syphilitic in type, whether it was nonspecific, whether it was due to a streptococcus or to some other bizarre lesion such as periarteritis nodosa, I do not see how we can say. However, I am inclined to explain the abdominal symptomatology on the same basis. If we do that, we are brought to a diagnosis of acute intestinal obstruction caused by intestinal infarction based on primary arterial disease. In addition, we know that the patient had carcinoma of the rectum. He probably had syphilis, and he had aortic regurgitation, myocarditis and hypertension.

This patient's course in the hospital bore out the judgment of those who had charge of the case. It is fair to say, however, that the evidence presented to us in the text makes it hard to see why they withheld operation at the time of admission to the hospital the second time. As a rule, early cases of acute intestinal obstruction are treated by fluid therapy, transfusion and operation, particularly when there is evidence that suggests strangulation, as in this case.

We are left to explain the mass in the left lower quadrant. If we make a diagnosis of intestinal infarction, we must assume that the mass was an infarcted, devitalized loop of intestine or a perforated loop with abscess. An unusual feature of this man's symptomatology at the second admission was the absence of vomiting. Usually, when there has been such a severe acute disturbance of bowel function, there is vomiting in connection with the cramplike pain. A diagnosis of intestinal infarction takes one "way out on a limb," but it seems to me that that is the most probable diagnosis in this particular case. The possibility that the patient had a lesion such as intussusception of the sigmoid, possibly in relation to a polyp, must be

considered, but I dismiss that from the diagnostic possibilities in my own mind.

DR. TRACY B. MALLORY: Dr. Stewart has brought out clearly the fact that this is a complicated case, the symptomatology of which certainly cannot be explained by the presence of carcinoma of the rectum, which we know the patient had.

DR. F. DENNETTE ADAMS: Would Dr. Stewart consider the possibility of a diverticulum above the cancer, with rupture at the time that the episode occurred?

DR. STEWART: I did consider that in going over the case. There were premonitory symptoms of two days' duration before the onset of the acute abdominal pain. Furthermore, an elevation of temperature at the time of the onset of abdominal pain suggests some general process or some inflammatory process apart from the acute lesion, but I do not see how we can make that diagnosis any more definite. I should be a little surprised to find that the patient had gas in the small intestine if the obstruction originated in the sigmoid, but I suppose it is a possibility.

CLINICAL DIAGNOSES

Carcinoma of the rectum.
Diverticulitis?
Ulcerative colitis?

DR. STEWART'S DIAGNOSES

Acute obstruction of the small intestine, due to infarction.
Carcinoma of the rectum.
Aortic regurgitation and chronic myocarditis.
Serologic syphilis.

ANATOMICAL DIAGNOSES

Diverticulitis of the sigmoid.
Carcinoma of the rectum.
Temporal arteritis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: So-called "temporal arteritis" is still a quite mysterious lesion. It is usually seen in people beyond the age of fifty, is generally bilateral and generally clears up spontaneously after varying lengths of time, and the histologic picture is rather characteristic. In the wall of the blood vessel, usually in the media, one finds considerable numbers of foreign-body giant cells, but to me the lesion does not look like periarteritis nodosa. It affects larger vessels than periarteritis nodosa usually does. It is a little more similar in appearance to the acute stage of Buerger's disease but again varies somewhat from that, and its uniform appearance in elderly people is very much against Buerger's disease. Whether patients suffering from temporal arteritis have similar vascular lesions elsewhere in the body is still unknown. I am not aware of any absolutely proved example, but it seems probable that they may occur.

DR. EDWARD F. BLAND: The Mayo Clinic[1] reported about a dozen cases, and as I recall there was no direct relation to syphilis in any of these, either histologically or clinically. In one case a radial artery was also suspected of being involved at the same time, but this was not definitely established. Dr. Adams had a patient here last year with this condition of temporal arteritis; I saw another patient last year, and one was reported at the Boston City Hospital[2] two years ago. They all followed the same clinical course and recovered after a period of months.

DR. MALLORY: In one case from which we had a biopsy specimen, the patient turned up later with intermittent claudication in the legs, but it was never possible to establish a diagnosis as to the vessels of the leg.

DR. RICHARD H. SWEET: At operation it was discovered, of course, that the small-bowel obstruction had disappeared. We noted that the tender mass was an area of diverticulitis of the sigmoid above and entirely separate from the cancer. The sigmoidal diverticulitis had perforated, and a thick inflammatory mass was adherent to the bladder. We did not see any evidence of fecal contamination. We therefore made a localized excision of that area with a proximal colostomy, brought the lower end below the sigmoidal lesion out in the lower portion of the wound, — somewhat as one does in the first stage of a Lahey excision of the rectum in two stages, — and left the rectal carcinoma to be dealt with later.

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The New England
Journal of Medicine
Formerly
The Boston Medical and Surgical Journal
Established in 1828

Owned by The Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year, Boston funds; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to *The New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

BIOPSY IN TUMOR DIAGNOSIS

Since the choice of surgery or radiation in the therapy of tumors hinges largely on an exact knowledge of the type of neoplastic cell present, biopsy is essential, even when one is reasonably sure that a tumor rather than another type of lesion is involved.

If the tumor is easily reached, incisional biopsy is usually simple and best suited to supply material for accurate diagnosis. Not always, however, is the tumor accessible; when it is deeply seated, one may resort to the aspiration of tumor cells or bits of tissue, and various methods have been suggested. One of the most satisfactory is that described in a paper in the present issue of the *Journal*. The procedure is one that traumatizes tissue but little and is fairly simple to carry out.

All methods of aspiration biopsy have certain inherent difficulties. Sometimes it is difficult to tell whether the tumor itself and not adjacent tissue has been removed. Furthermore, since the diagnosis of the pathologist frequently depends not only on the types of cells but also on the relation of tissues, a clear idea of general structure and tissue relation can be obtained only with difficulty from small amounts of tissue. This disadvantage is particularly great in cases of tumors of the breast or of the bone. Pathological diagnosis based on tissue removed by aspiration of various types should be guarded, and the findings should be weighed carefully with the clinical and roentgenographic evidence.

THE PROBLEM OF THE THREE EDWARD WARRENS

When three men, all living at the same time, and all making distinct contributions to American medical literature, have the same name, without middle initials, the bibliographic confusion a hundred years later is not inconsiderable. When one, moreover, is closely associated with the ether controversy, another writes concerning the life of the man who, next to Morton, played the leading role in the ether demonstration in 1846 and a third became an Egyptian *Bey*, the demand becomes insistent to identify the individuals and their works. The problem, in part, was solved correctly four decades ago in the Army Medical Library; nevertheless, such are the vagaries of mind and the unreliability of man that the same institution now falls into error, and the world of bibliography must be again set right. To do so, however, is not by any means easy. Of one Edward Warren we know much, of another a moderate amount, but of the third, who gives the most difficulty, we know scarcely anything.

The easiest problem concerns the Edward Warren (1828–1893), *Bey*, a romantic Virginian, one of the most bizarre figures in the annals of American medicine, whose life has been well summarized by Howard A. Kelly in the *Dictionary of American Medical Biography* (1928). Born in 1828, in North Carolina, he became, in order, a country

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doctor, a medical editor, a professor of surgery, a medical inspector of the confederate states during the Civil War, the chief surgeon of the general staff of Ismail Pasha in Egypt, a practitioner in Paris and a chevalier of the Legion of Honor. After a life on three continents he settled in Paris, and died there in 1893. An account of his unusual adventures is told in his book, *A Doctor's Experiences in Three Continents* (Baltimore, 1885), which consists of a series of letters to his friend, Dr. John Morris, of Baltimore. Known as Edward Warren, *Bey*, he is easily identified and correctly referred to in the first series of the *Index-Catalogue*. Unfortunately, he is confused with another Edward Warren in the third series of the same great catalogue. His picturesque career, unique in American medicine, and based on his work in the swamps of Carolina, on the shores of the Chesapeake, on the borders of the Nile and in the *quartiers* of the Seine, has been thoroughly depicted in numerous biographical sketches of the man. The *Bey* was not a contributor to the literature of the ether controversy, nor was he related, except possibly distantly, to the Warren family of Boston.

The other two Warrens with the given name of Edward were both Warrens of New England. The better known was Edward Warren (1804–1878), younger brother of the John Collins Warren (1778–1856) who performed the ether operation at the Massachusetts General Hospital on October 16, 1846. His well-known *Life of John Collins Warren* (Boston, 1860) was published in two volumes. He also wrote a biography of his father, *Life of John Warren, M.D.* (Boston, 1874). The reference to this book is the one incorrectly given in the third series of the *Index-Catalogue*. This Edward Warren graduated from Harvard College in 1826 and the Harvard Medical School in 1829, won the Boylston Prize in 1838 and in 1839 and, as noted above, wrote two important biographies. He was not a member of the Massachusetts General Hospital staff in 1846, and although forty-two years old at the time, there is no record of his being in the hospital on October 16 of that year. He took no part in the ether controversy, although he wrote an admirable account of it a decade later in the biography of his elder brother. This Edward Warren is most often confused with Edward Warren, *Bey*.

The identity of the third Edward Warren forms the real problem. His name stands out clearly on an important and rare ether pamphlet, *Some Account of the Letheon; or, Who Was the Discoverer?* (Boston, 1847). A second and a third edition, with a slight change in the title, were also issued in 1847. This publication by Warren must not be confused with the pamphlet by W. T. G. Morton, *Circular, Morton's Letheon* (Boston, 1846), five editions of which were issued in 1846 and 1847, this being Osler's first anesthesia item in his "Bibliotheca Prima," published in *Bibliotheca Osleriana* (Oxford, 1929). The Warren pamphlet was issued by Edward Warren, Morton's business associate and, according to Ford, a nephew of John Collins Warren. He came from Palmyra, Maine, and was closely associated with Morton during the early days of ether anesthesia. He is the same Edward Warren who contributed to the April 28, 1847, issue of the *Boston Medical and Surgical Journal* a note, "The Letheon and Dr. Wells" and to the May 19, 1847, issue a letter, "Ethereal Inhalation: Dr. Wells's claims as discoverer." The first of these two notes aroused the interest of Edward Warren, the physician and brother of John Collins Warren, who in a letter in the July 21, 1847, issue of the *Boston Medical and Surgical Journal* stated that he was not the author of the article, but that it was written by "a *non*-medical gentleman connected in this business with Mr. Morton." Dr. Warren, moreover, stated that his sympathies were entirely with Dr. Jackson, thus at that time differing from his older brother, the surgeon at the first operation.

This "non-medical gentleman" was referred to as "Mr. Morton's *agent*," an epithet he vehemently protested against in the July 28, 1847, issue of the *Boston Medical and Surgical Journal*. Little more is known of this third Edward Warren, not a physician in 1846, but whose name is so intimately associated with that of Morton. We can at least dissociate him from the *Bey* and from the

biographer. There are other unsolved questions, however, and it is hoped that light will be thrown on them by the work of Dr. William W. Ford, whose long-anticipated book on the life of Morton was nearing completion at the time of his death.

MEDICAL EPONYM

Howell-Jolly Bodies

In an article entitled "The Life-History of the Formed Elements of the Blood, Especially the Red Blood Corpuscles" and published in the *Journal of Morphology* (**4**: 57–116, 1890), William Henry Howell (b. 1860), professor of physiology and histology, University of Michigan, described these as follows:

> I have met with corpuscles containing granulations very frequently. . . . Sometimes the granules — which stain, by the way, like nuclear chromatin — are so arranged as to represent the outline of the nucleus. . . . There is no evidence to show that the granules are the last remaining fragments of an absorbed nucleus. . . . They must be looked upon, it seems to me, as bits of the nuclear chromatin (membrane) left behind when the nucleus leaves the cell.

J. Jolly, in a monograph entitled "Recherches sur la formation des globules rouges des mammifères [Studies in the Formation of Red Cells in Mammals]," which was published in the *Archives d'Anatomie Microscopique* (**9**: 133–314, 1907), repeatedly refers to similar bodies.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Placenta Previa and Rupture of the Uterus, Followed by Hemorrhage and Death

A forty-one-year-old para IX was sent into the hospital as an emergency case, when approximately thirty-five weeks pregnant. She had been bleeding off and on for three or four days and had had no prenatal care.

Physical examination disclosed an undernourished woman who was bleeding freely from the vagina. The uterus was enlarged to about the size of a thirty-five-week pregnancy, and the fetal heart was audible. One hour after entrance, the vagina was packed with gauze. On the following morning, a consultation was held. The pack was removed; a Lysol douche was given, and examination presumably revealed no placenta previa, because the patient was allowed to get up and prepared to go home. When she was about to leave the hospital, she again began to bleed freely. Another douche was given, and the patient was put to bed. The next day a diagnosis of marginal placenta previa was made, and a Voorhees bag inserted. Since labor did not start immediately, one ampule of posterior pituitary extract was given four hours after the insertion of the bag. Good labor did not result, and the bag was not expelled until fifty-two hours after it had been inserted. Another Lysol douche was given, and a podalic version and breech extraction, with manual removal of the placenta, were performed. The version was said to have been easy. The baby was stillborn. The amount of bleeding following the removal of the placenta was reported as surprisingly little, in spite of which the patient went into deep shock and died an hour and forty-two minutes after delivery.

Comment. The absence of prenatal care in no way influenced the course of this particular patient, since no matter how carefully prenatal care is observed it cannot prevent placenta previa and its subsequent bleeding. At the first examination when no placenta was felt, the cervix was probably not investigated. Had the finger been put inside the cervix, the placenta would have been felt. At that time a bag might have been introduced, a procedure which would have prevented the subsequent hemorrhage. Vaginal packing for the treatment of uterine hemorrhage late in pregnancy has no place in good obstetrics unless the membranes are ruptured and a Spanish windlass applied, as is customary when placenta ablatio is diagnosed. Lysol douches have no value in obstetrics. One must always realize that when a bag is inserted at this stage of pregnancy, it may take quite some time before labor starts. If the cervix were fully dilated when the bag was expelled, it is rather difficult to understand why a version at this stage of pregnancy would have been difficult. When a bag is used for controlling hemorrhage in any type of previa, it is usually wise to finish the delivery when the bag is extruded. If the cervix is not fully dilated, a Braxton-Hicks maneuver is the safest procedure. It is very likely that this uterus was ruptured at the time of delivery, for in the absence of much external bleeding the com-

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

monest cause of death so soon after delivery is hemorrhage into the peritoneal cavity from rupture of the uterus, with subsequent shock.

It is reported that in this case one ampule of pituitary extract was given after the bag had been introduced. This is very poor obstetrics. Minim doses repeated at regular intervals can do no harm, but an ampule at any time during labor before the baby and placenta are delivered is not advisable.

DEATH

OSBORNE — EDWARD D. OSBORNE, M.D., of New Bedford, died May 19. He received his degree from Howard University College of Medicine in 1907. He was a member of the Massachusetts Medical Society and the American Medical Association.

His sister survives him.

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MISCELLANY

TUBERCULOSIS IN MENTAL HOSPITALS

Dust swept under the sofa disturbs no one — until it is discovered; nor does tuberculosis hidden from public view. It is well to be reminded that more than 5 per cent of the people who die of tuberculosis annually in the United States are in mental hospitals. Scant attention has been paid to this sector of the problem, for which reason an article on tuberculosis in mental hospitals (Pollak, M., Hummel, A. V., and Turow, I. L. Tuberculosis in mental hospitals. *Am. Rev. Tuberc.* **43**:373–382, 1941) commands the attention of health workers, hospital authorities and physicians. An abstract of the article follows.

The Peoria (Illinois) State Hospital, with an average daily census of 2575 patients, has had a tuberculosis division since 1905. X-ray examination of the 56 patients assigned to it showed that 16 per cent had no tuberculosis. Thus, of the resident patients in the hospital at the beginning of the survey, only 47 (1.87 per cent) were known to have tuberculosis.

From the beginning of the survey it was obligatory to take a chest roentgenogram on all patients who were transferred to the infirmaries, irrespective of whether tuberculosis was suspected or not. In the course of the study there were surveyed 2156 patients in residence, 766 newly admitted patients and 477 employees. Tuberculin tests of these groups (all but about 4 per cent were tested with tuberculin) showed positive reactions in 94.6 per cent of resident patients, 80.6 per cent of receiving-ward patients and 57.3 per cent of the employees. Parenchymal lesions were revealed by x-ray examination in 11.2 per cent of resident patients, 7.4 per cent of receiving-ward patients and 1.6 per cent of employees. The majority of the resident patients and less than half the receiving-ward patients were over fifty years old. The great majority of employees were under fifty years of age.

The percentage of the tuberculous increased with the length of stay of the patients. Of the tuberculous employees, one half developed the disease after five years of service.

About 10 per cent of the tuberculous patients in the receiving wards were committed from tuberculosis sanatoriums and about 14 per cent were known to have tuberculosis at the time of admission. The remaining cases were discovered in the course of the survey.

This study bears out what has been found in other studies, namely, that when the physical examination alone is depended on, tuberculosis is at times diagnosed when it does not exist and overlooked at others even in the terminal stage. One investigator found that 38 per cent of the patients on the tuberculosis wards had no tuberculosis. In another hospital for mental diseases, 2 undiagnosed cases were found in 50 autopsies.

The different infection rates in the three groups can be attributed to the different age groups, and the high percentage of positive reactors among the resident patients chiefly to advanced age. It should be considered also that patients in this study come largely from the low-income group, in which infection and morbidity rates are known to be high.

The significant difference in the percentage of tuberculosis among resident (11.2 per cent) and receiving-ward (5.7 per cent) patients indicates that many of the patients develop tuberculosis while they reside in the institution.

> The rationale of spending money on tuberculosis prevention among the psychotics, who already represent a tremendous burden on society, was seriously questioned by some authorities in the course of our study. The fact, however, that 6.9 per cent of our tuberculous patients have already been discharged or paroled by January 1, 1940, shows that some of these patients have an opportunity to spread their disease in their own family and community after they return home. The possibility of the spread of the disease from these patients to the employees has also to be considered seriously. For these reasons the money spent on tuberculosis prevention must be considered as a prudent investment on the part of hospital authorities.

The treatment of the tuberculous psychotic differs in no way from that of the mentally normal, namely, rest. The chief aim of treatment is to produce a negative sputum, and, therefore, collapse therapy is used even if the patient's mental condition seems to be entirely hopeless. Patients under shock therapy deserve special consideration — 3.2 per cent of such patients developed tuberculosis either during the course or after the treatment. Patients should be x-rayed immediately before undergoing shock therapy and frequently thereafter.

Should tuberculous psychotics be centralized in one institution? The disadvantage (from the state's standpoint) is that the transportation of patients is costly and that it entails a hardship when the family of a patient has to travel a long distance. Under decentralization, each hospital has to have on its staff at least one physician who is well trained in psychiatry as well as phthisiotherapy. The training of such physicians promises worthwhile contributions to the psychiatric as well as to the tuberculosis field.

The author's conclusions are as follows:

> Tuberculosis is a problem of first order in every mental institution.
>
> Patients suffering from tuberculosis are admitted to these institutions in a fairly large percentage without being so diagnosed. In addition to these, a relatively large percentage of patients develop tuberculosis while in residence, again without their disease being recognized.
>
> Owing to the contagious nature of tuberculosis, mental institutions should develop a definite and systematic tuberculosis-control program, employing the tuberculin test and x-ray study in diagnosis. These examinations should be conducted on all newly ad-

mitted patients immediately after admission and on the resident patients at least once annually.

Collapse therapy should be fully utilized in the treatment of the tuberculous psychotic, irrespective of the patient's mental deterioration.

Patients selected for shock therapy should be x-rayed before treatment is begun and re-rayed at frequent intervals during and after such treatment.

Employees coming in close contact with the patients should be x-rayed every three months, and the tuberculin reactors among the other personnel at least once annually. — Reprinted from *Tuberculosis Abstracts* (June, 1941).

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1941

Diseases	April 1941	April 1940	Five-Year Average*
Anterior poliomyelitis	1	0	0
Chicken pox	1181	1286	1139
Diphtheria	16	11	14
Dog bite	1314	907	937
Dysentery, bacillary	1	24	9
German measles	522	56	211
Gonorrhea	315	368	412
Lobar pneumonia	391	521	573
Measles	4018	2463	3303
Meningococcus meningitis	8	5	15
Mumps	1492	756	1106
Paratyphoid B fever	6	3	9
Scarlet fever	877	756	1111
Syphilis	419	479	498
Tuberculosis, pulmonary	287	189	298
Tuberculosis, other forms	29	19	32
Typhoid fever	2	10	5
Undulant fever	13	4	3
Whooping cough	807	625	726

*Based on figures for preceding five years.

RARE DISEASES

Anterior poliomyelitis was reported from: Pittsfield, 1; total, 1.

Diphtheria was reported from: Fall River, 1; Foxboro, 1; Northbridge, 1; Saugus, 3; Springfield, 4; Tyngsboro, 1; Waltham, 2; West Springfield, 1; Worcester, 1; total, 15.

Dysentery, amebic, was reported from: Worcester, 1; total, 1.

Dysentery, bacillary, was reported from: Framingham, 1; total, 1.

Infectious encephalitis was reported from: Dedham, 1; Scituate, 1; Winthrop, 1; total, 3.

Malaria was reported from: Fort Banks, 1; total, 1.

Meningococcus meningitis was reported from: Boston, 1; Camp Edwards, 1; Milton, 1; Springfield, 1; Wareham, 1; Worcester, 3; total, 8.

Paratyphoid B fever was reported from: Haverhill, 1; Malden, 3; Salem, 2; total, 6.

Pellagra was reported from: Winchendon, 1; total, 1.

Pfeiffer bacillus meningitis was reported from: Framingham, 1; total, 1.

Septic sore throat was reported from: Andover, 1; Beverly, 3; Boston, 10; Fall River, 4; Framingham, 1; Hanson, 2; Lynn, 1; Milton, 1; total, 23.

Tetanus was reported from: Swampscott, 1; total, 1.

Trachoma was reported from: Boston, 1; Lynn, 1; total, 2.

Typhoid fever was reported from: Chelsea, 1; New Bedford, 1; total, 2.

Typhus fever was reported from: Chelmsford, 1; total, 1.

Undulant fever was reported from: Acton, 1; Adams, 1; Amherst, 1; Leominster, 6; Lowell, 1; Littleton, 1; Montague, 1; Walpole, 1; total, 13.

The second case of anterior poliomyelitis for the year was reported in April.

Chicken pox, diphtheria and whooping cough were reported slightly above the five-year averages.

Dog bite, which has been increasing steadily since January, showed a record high figure for this month.

Bacillary dysentery showed low incidence.

Lobar pneumonia was reported at the lowest figure since the corresponding month in 1933.

Mumps and German measles were reported highest in any month since 1936.

Measles, which has been climbing steadily since October, was reported still above the five-year average.

Meningococcus meningitis, typhoid fever, paratyphoid B fever, tuberculosis (pulmonary), and tuberculosis (other forms) were reported below the five-year averages.

Undulant fever showed an all-time record high figure for any one month.

Scarlet fever, which has been climbing since August, was reported below the five-year average.

NOTICES

ANNOUNCEMENT

Dr. Robert L. Mason announces the removal of his office from 12 Bay State Road, Boston, to 75 Bay State Road, Boston.

MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

Medical Inspector, School Department, $500 a Year, Westfield

Director of State Civil Service, Ulysses J. Lupien, has announced that competitive examinations are to be held on July 22 to find eligibles for appointment to the position of medical inspector, School Department, Westfield.

The entrance requirement is as follows: applicants must be registered physicians under the Massachusetts Board of Registration in Medicine. The subjects and weights of the examination are as follows: training and experience, 2; practical questions, 3; total, 5. Applicants must obtain a grade of 70 per cent in each subject in order to become eligible. The last date for filing applications is Tuesday, July 1, at 5 p.m.

MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

School Physician, School Department, $1000 a Year, Leominster

Director of State Civil Service, Ulysses J. Lupien, has recently announced that a competitive examination is to be held on July 25 in order to find eligibles for appointment to the position of school physician, School Department, Leominster.

The entrance requirement is as follows: applicants must be registered physicians under the Massachusetts Board of Registration in Medicine. The subjects and weights of the examination are as follows: training and experience, 2; practical questions, 3; total, 5. Applicants must obtain a grade of 70 per cent in each subject in order to become eligible. The last date for filing applications is Monday, July 7, at 5 p.m.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories (Part I) for Group B candidates will be held in various cities of the United States and Canada on Saturday, January 3, 1942, at 2:00 p.m. Candidates who successfully complete the Part I examinations proceed automatically to the Part II examinations held later in the year. Applications for admission to Group B, Part I, examinations must be on file in the secretary's office not later than October 6, 1941. Applications for Group A must be in the secretary's office by March 1, 1942.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire board, meeting at Atlantic City, New Jersey, immediately prior to the 1942 meeting of the American Medical Association.

As previously announced in the board booklet, this fiscal year (1941–1942) of the board marks the close of the two groups of classification of applicants for examination. Thereafter, the board will have only one classification of candidates, and all will be required to take the Part I and Part II examinations. For further information and application blanks, address Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, JUNE 22

MONDAY, JUNE 23

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, JUNE 24

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, JUNE 25

*12 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

JUNE 22–24 — Maine Medical Association. Marshall House, York Harbor, Maine.

SEPTEMBER 1–5 — American Congress of Physical Therapy. Page 997, issue of June 5.

SEPTEMBER 1–5 — American Occupational Therapy Association. The Mayflower, Washington, D. C.

OCTOBER 13–24 — 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

OCTOBER 14–17 — American Public Health Association. Page 579, issue of March 27.

JANUARY 3, 1942 — American Board of Obstetrics and Gynecology. Notice above.

APRIL 20–24 — American College of Physicians. Page 996, issue of June 5.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Story of Clinical Pulmonary Tuberculosis. By Lawrason Brown, M.D. 8°, cloth, 411 pp., with 1 portrait. Baltimore: Williams and Wilkins Company, 1941. $2.75.

A Manual of Allergy for General Practitioners. By Milton B. Cohen, M.D., director of the Asthma, Hay Fever and Allergy Foundation; visiting physician in allergy, St. Alexis Hospital, Cleveland, Ohio. 12°, cloth, 156 pp. New York: Paul B. Hoeber, Incorporated, 1941. $2.00.

Arthritis and Allied Conditions. By Bernard I. Comroe, A.B., M.D., instructor in medicine, University of Pennsylvania; senior ward physician, Hospital of the University of Pennsylvania. Second edition, thoroughly revised. 8°, cloth, 878 pp., with 242 illustrations. Philadelphia: Lea and Febiger, 1941. $9.00.

A Textbook of Dietetics. By L. S. P. Davidson, B.A. (Cantab.), M.D. (Edin.), F.R.C.P. (Edin. and Lond.), F.R.S.E., professor of medicine and clinical medicine in the University of Edinburgh and physician to the Royal Infirmary, Edinburgh; and Ian A. Anderson, M.B., Ch.B. (Aberd.), clinical tutor and assistant in the metabolic wards, the Royal Infirmary, Aberdeen. With diet sheets constructed by Miss Mary E. Thomson, S.R.N., sister dietitian to the Royal Infirmary, Aberdeen, and a foreword by Sir John Boyd Orr, M.D., D.Sc., LL.D., F.R.S., director, Rowett Institute for Research in Animal Nutrition, Aberdeen. 8°, cloth, 324 pp., with 27 tables. New York: Paul B. Hoeber, Incorporated, 1941. $4.25.

Scabies — Civil and Military: Its prevalence, prevention and treatment. By Reuben Friedman, M.D., assistant professor of dermatology and syphilology, Temple University School of Medicine, Philadelphia. 8°, cloth, 288 pp. New York: Froben Press, 1941. $3.00.

Brucellosis (Undulant Fever): Clinical and subclinical. By Harold J. Harris, M.D., health officer, Westport, New York, consulting physician, St. Lawrence State Hospital, and attending physician, Elizabethtown Community Hospital. With a foreword by Walter M. Simpson, M.D., director, Kettering Institute for Medical Research, Miami Valley Hospital, Dayton, Ohio. 8°, cloth, 286 pp., with 12 colored and 44 black-and-white illustrations. New York: Paul B. Hoeber, Incorporated, 1941. $5.50.

The Medical Aspect of Boxing. By Ernst Jokl, M.D., head of Department of Physical Education, Witwatersrand Technical College, Johannesburg, South Africa; consultant, Medical Aspect of Physical Education, South Africa Defense Force. 8°, cloth, 251 pp., with 55 illustrations and 4 plates. Pretoria, South Africa: J. L. Van Schaik, Limited, 1941.

Medical Diagnosis and Symptomatology. By Samuel A. Loewenberg, M.D., clinical professor of medicine, Jefferson Medical College, assistant physician, Jefferson Hospital, consulting physician, Philadelphia Hospital for Contagious Diseases and Philadelphia Psychiatric Hospital, and visiting physician, Philadelphia General Hospital and Northern Liberties Hospital. Fifth edition, entirely revised and reset. 4°, cloth, 1139 pp., with 520 illustrations. Philadelphia: F. A. Davis Company, 1941. $12.00.

The Doctor Takes a Holiday: An autobiographical fragment. By Mary McKibbin-Harper, M.D. 8°, cloth, 349 pp., with 17 illustrations. Cedar Rapids, Iowa: The Torch Press, 1941. $2.50.

Medicine. No. 4 in the series, *Vocational and Professional Monographs.* By Dwight O'Hara, M.D., professor of preventive medicine and assistant dean, Tufts College Medical School, Boston. 8°, paper, 27 pp. Boston: Bellman Publishing Company, Incorporated, 1941. 50c.

Oral Pathology: A histological, roentgenological and clinical study of the diseases of the teeth, jaws and mouth. By Kurt H. Thoma, D.M.D., professor of oral surgery and Charles A. Brackett Professor of Oral Pathology, Harvard University. 4°, cloth, 1306 pp., with 1370 illustrations, including 137 in color. St. Louis: The C. V. Mosby Company, 1941. $15.00.

The Medical Clinics of North America: New York number, May, 1941. Vol. 25, No. 3. 8°, cloth, 265 pp. Philadelphia: W. B. Saunders Company, 1941. $3.00.

Mary Fletcher Comes Back: A brief account of the history, progress and future of Vermont's first general hospital. 4°, cloth, 68 pp., with 37 illustrations. Burlington, Vermont: published for the Board of Directors of The Mary Fletcher Hospital, 1941.

Über die Bedeutung der Röntgenuntersuchung für die Kardiologie: Speziell mit Rücksicht auf die Bedeutung der Herzvergrösserung. By Torfinn Denstad. 8°, paper, 80 pp., with 16 illustrations, and 19 tables. Stockholm: P. A. Norstedt und Söner, 1941. Sw. Cr. 8.

BOOK REVIEWS

Manual of the International List of Causes of Death. Based on the fifth decennial revision by the International Commission, Paris, October 3–7, 1938. *Manual of Joint Causes of Death.* Fourth edition, 1939. Prepared under the supervision of Halbert L. Dunn, M.D. 8°, cloth, 452 pp. Washington: United States Government Printing Office, 1940. $1.25.

These two new editions of standard works, published as a unit, should be of interest to all those engaged in the classification of diseases and in biologic research.

Chemistry and Medicine: Papers presented at the fiftieth anniversary of the founding of the Medical School of the University of Minnesota. Edited by Maurice B. Visscher. 8°, cloth, 296 pp., with 76 figures and 19 tables. Minneapolis: The University of Minnesota Press, 1940. $4.50.

In formulating an appropriate program for the commemoration of the fiftieth anniversary of the University of Minnesota Medical School, it was decided to focus the scientific program on chemistry as it is related to medicine. The papers thus presented were of such excellence that they were published under the direction of Dr. Maurice Visscher. Fourteen papers, embracing such fields as the application of physical chemistry to medicine, recent investigations in metabolism, aspects of immunity and chemotherapy, and certain approaches to the nervous control of the organism, and including such subjects as heparin and thrombosis, and the chemistry of urinary antisepsis, make this collection of data and well-digested review material by distinguished investigators outstanding in every respect. The book is recommended enthusiastically not only to those in specialized branches of medicine but also to all who are interested in modern medicine. The synthesis of each subject as it is developed is so well done that the collection merits being termed the best symposium book of the year.

The Doctor and the Difficult Child. By William Moodie, M.D. 8°, cloth, 214 pp. New York: The Commonwealth Fund, 1940. $1.50.

The author treats this subject in a very simple and wholesome manner. He very wisely avoids attempting to lead the physician into the more recently explored psychologic fields, which offer a rare opportunity for many authors to philosophize and speculate on imaginary situations. The book sticks to the task of thinking "of the patients just as individuals, differing one from another in themselves, their experiences and their setting, and so varying widely in their methods of thinking and acting." Clearly and concisely, the author presents and evaluates the problems of childhood, and then discusses therapeutic measures as they may be applied directly to the child and indirectly toward the environment. Although the book represents the orthodox approach to behavior problems and personality deviations, as carried on in most of the child-guidance clinics, it will have special value for the physician whose practice brings him in contact with the ordinary problems associated with the process of growing up.

The Era Key to the USP XI and NF VI. Fifth edition. Revised by Lyman D. Fonda, professor of pharmacy, Brooklyn College of Pharmacy, Long Island University. 16°, cloth, 320 pp. Newark, N. J.: Haynes and George Company, Incorporated, 1939. $1.00.

This is the fifth edition of a popular book that has been in existence for forty-six years. It is small and compact in arrangement, and is designed to give the essential information contained in the *United States Pharmacopoeia* and in the *National Formulary*.

As I Remember Him: The biography of R. S. By Hans Zinsser, M.D., S.D. 8°, cloth, 443 pp. Boston: Little, Brown and Company, 1940. $2.75.

This biography of a physician is essentially an attempt by a representative of the educated middle class to draw a picture of the period of transition between the nineteenth and twentieth centuries. The story, beginning with childhood, is carried through his career as a medical bacteriologist in Serbia, France, Russia, China and Japan, and ends with thoughts on the fact that he would soon be dead.

The style of writing is vigorous, but frequently unconventional and choppy. One finds interesting anecdotes and incisive phrases, such as, "The whole publicizing of culture is a racket." The author attacks those who want education "in hypodermics or like liver extract." In his discussion of the philosophical aspects of life the author finds no hope in achieving a physicochemical basis for human morality, nor does he seek strength in wishful surrender to a religious faith. Despite these mental confusions he acquires a certain degree of philosophical tranquillity and resignation in the last months of his life. Those interested in the history of medicine, as well as others, will find many good things to reflect on in reading this book.

A Textbook of Physiology. By William H. Howell, Ph.D., Sc.D., LL.D. Fourteenth edition, thoroughly revised. 8°, cloth, 1117 pp., with 330 illustrations. Philadelphia and London: W. B. Saunders Company, 1940. $7.50.

The first issue of this textbook appeared thirty-five years ago. Since that time, the distinguished author has reflected in subsequent editions the spirit and accomplishments of contemporary physiology. The textual material is incorporated under the influence of two guiding principles: the presentation of facts and theories in simple, lucid style, and the exercise of judicious limitations in the selection of such material as has been justified by experiment and observation. Throughout, the author attempts to show that physiology is a living subject, continually undergoing change and adjustment. The short résumés of the literature and the attention paid to works of historical importance enhance the value of the book.